STIC Search

Inventor Search



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L17 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:323156 HCAPLUS
DOCUMENT NUMBER: 129:19687
TITLE: Acellular pertussis vaccine with diphtheria and tetanus toxoids
INVENTOR(S): **Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian**
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S. A., Belg.; Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9819702 | A1 | 19980514 | WO 1997-EP6180 | 19971104 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9853196 | A1 | 19980529 | AU 1998-53196 | 19971104 |
| AU 710475 | B2 | 19990923 | | |
| EP 941117 | A1 | 19990915 | EP 1997-950137 | 19971104 |
| EP 941117 | B1 | 20020828 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI | | | | |
| CN 1236321 | A | 19991124 | CN 1997-199491 | 19971104 |
| BR 9712917 | A | 19991207 | BR 1997-12917 | 19971104 |
| NZ 335384 | A | 20001027 | NZ 1997-335384 | 19971104 |
| JP 2001503422 | T2 | 20010313 | JP 1998-521070 | 19971104 |
| AT 222773 | E | 20020915 | AT 1997-950137 | 19971104 |
| EP 1240905 | A1 | 20020918 | EP 2002-75821 | 19971104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI | | | | |
| ES 2182131 | T3 | 20030301 | ES 1997-950137 | 19971104 |
| ZA 9709984 | A | 19980723 | ZA 1997-9984 | 19971106 |
| TW 471971 | B | 20020111 | TW 1997-86119712 | 19971224 |
| NO 9902156 | A | 19990504 | NO 1999-2156 | 19990504 |
| KR 2000053092 | A | 20000825 | KR 1999-704016 | 19990506 |
| MX 9904278 | A | 20000131 | MX 1999-4278 | 19990507 |
| US 2001014331 | A1 | 20010816 | US 2001-827785 | 20010406 |

PRIORITY APPLN. INFO.:
GB 1996-23233 A 19961107
EP 1997-950137 A3 19971104
WO 1997-EP6180 W 19971104
US 1999-284887 B1 19990527

AB The invention provides a diphtheria, tetanus and pertussis vaccine comprising a low dose of each of diphtheria toxoid (D), tetanus toxoid (T), pertussis toxin (PT), filamentous hemagglutinin (FHA) and pertactin (69K). The vaccine maintains an ability to prevent pertussis while showing exceptionally low reactogenicity. Combination vaccines comprising addnl. antigens are also provided.

IC ICM A61K039-10
ICS A61K039-05; A61K039-08
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15
ST vaccine pertussis diphtheria tetanus toxoid formulation
IT Hepatitis
(A, immunity to; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Hemagglutinins
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(FHA (filamentous hemagglutinin); acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Pertussis
Vaccines
(acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Immunostimulants
(adjuvants; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Toxoids
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(diphtheria; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Antigens
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hepatitis B surface; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Poliomyelitis
(immunity to; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Agglutinins and Lectins
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pertactins; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Antigens
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pertussis; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT Toxoids
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(tetanus; acellular pertussis vaccine with diphtheria and tetanus toxoids)
IT 7784-30-7, Aluminum phosphate 21645-51-2, Aluminum hydroxide, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant; acellular pertussis vaccine with diphtheria and tetanus toxoids)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d que stat l22
L14           2 SEA FILE=REGISTRY ABB=ON  "ALUMINUM PHOSPHATE"/CN
L15           1 SEA FILE=REGISTRY ABB=ON  "ALUMINUM HYDROXIDE"/CN
L16          18 SEA FILE=HCAPLUS ABB=ON  ?DIPHTHERIA? AND ?PERTUSSIS? AND
                ?TETANUS? AND (FHA? OR ?FILAMENT?(W)?HEMAGGLUT?) AND (?PERTACTI
                N? OR 69K)
        7 SEA FILE=HCAPLUS ABB=ON  L16 AND ?HEPATITIS?
L19           1 SEA FILE=HCAPLUS ABB=ON  L16 AND ?ANTIGEN?(3A)HBS?
L20           3 SEA FILE=HCAPLUS ABB=ON  L16 AND ?IMMUN?(3A)(HIB? OR ?POLIO?
                OR ?HEPATITIS?(W)A)
L21           4 SEA FILE=HCAPLUS ABB=ON  L16 AND (L14 OR ?ALUMINUM?(W)?PHOSPHAT
                ? OR L15 OR ?ALUMINUM?(W)?HYDROXID?)
L22          18 SEA FILE=HCAPLUS ABB=ON  L16 OR L18 OR L19 OR L20 OR L21

=> d ibib abs hitrn l22 1-18

L22  ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:341356  HCAPLUS
DOCUMENT NUMBER:          139:83492
TITLE:                    DTPa-HBV-IPV/Hib vaccine (Infanrix hexa)
AUTHOR(S):                Curran, Monique P.; Goa, Karen L.
CORPORATE SOURCE:         Adis International Limited, Auckland, N. Z.
SOURCE:                   Drugs (2003), 63(7), 673-682
                          CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER:                Adis International Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  Primary vaccination of infants with diphtheria-
     tetanus-acellular pertussis-hepatitis B
     recombinant (adsorbed)-inactivated poliomyelitis-adsorbed conjugated
     Haemophilus Influenzae type b vaccine (DTPa-HBV-IPV/Hib; Infanrix hexa)
     provided high levels of seroprotection against diphtheria
     toxoid, tetanus toxoid, poliovirus 1, 2 and 3, pertussis
     antigens (pertussis toxoid, filamentous
     hemagglutinin and pertactin), hepatitis B
     virus surface antigen and H. influenzae polyribosyl-ribitol-phosphate
     (PRP) antigen.  Most infants (97%) had anti-PRP levels .gtoreq. 0.15
     .mu.g/mL, after a booster dose at 18 mo.  Primary vaccination with the
     DTPa-HBV-IPV/Hib vaccine produced a similar immune response to that with
     two different pentavalent plus monovalent vaccine combinations.
     Coadministration of DTPa-HBV-IPV/Hib vaccine and a heptavalent
     pneumonococcal conjugate vaccine resulted in a high level of
     seroprotection and was well tolerated.  Primary or booster vaccination
     with DTPa-HBV-IPV/Hib vaccine was well tolerated.  Commonly reported local
     adverse reactions included redness, pain and swelling.  Systemic symptoms
     were usually mild to moderate, and included fussiness, fever, restlessness
     and sleepiness.
REFERENCE COUNT:          42    THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22  ANSWER 2 OF 18  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:300440  HCAPLUS
DOCUMENT NUMBER:          138:319681
TITLE:                    Genetically-detoxified pertussis holotoxin
                          as proteinaceous adjuvant
INVENTOR(S):              Gajewczyk, Diane M.; Boux, Heather A.; Novak, Anton;
                          Klein, Michel H.
PATENT ASSIGNEE(S):       Can.
SOURCE:                   U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U.S.
                          Ser. No. 258,228.
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CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003072774 | A1 | 20030417 | US 1995-481878 | 19950607 |
| CA 2192454 | AA | 19951221 | CA 1995-2192454 | 19950608 |
| EP 1149588 | A1 | 20011031 | EP 2001-201598 | 19950608 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1149589 | A1 | 20011031 | EP 2001-201610 | 19950608 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| ES 2179105 | T3 | 20030116 | ES 1995-924122 | 19950608 |

PRIORITY APPLN. INFO.: US 1994-258228 A2 19940610
EP 1995-924122 A3 19950608

AB A modulated immune response to an antigen is achieved by coadministering the antigen and a genetically-detoxified **pertussis** holotoxin, particularly one retaining its immunogenicity, to a host. The modulated immune response enables immunogenic compns., including multivalent pediatric vaccines, such as DTP, to be provided which produce a modulated immune response in the absence of extrinsic adjuvants, such as alum. The adjuvanting effect achieved by the genetically-detoxified **pertussis** holotoxin enables at least the same level of a modulated immune response to a non-Bordetella antigen to be achieved as previously attained by alum, without the undesirable side effects thereof. Modifications are possible within the scope of the disclosed invention.

L22 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:725623 HCAPLUS
DOCUMENT NUMBER: 137:215395
TITLE: Differing protective effects of acellular **pertussis** vaccines in neonatal and young mice in a murine model of respiratory infection
AUTHOR(S): Watanabe, Mineo; Komatsu, Eiji; Sato, Takaaki; Nagai, Masaaki
CORPORATE SOURCE: Division of Bacterial Vaccines, Research Center for Biologicals, The Kitasato Institute, Kitamoto, 364-0026, Japan
SOURCE: Journal of Health Science (2002), 48(4), 341-345
CODEN: JHSCFD; ISSN: 1344-9702
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The protective effects on neonatal (3.5 wk old) and young mice (7 wk old) of eight **pertussis** vaccines prepd. from various components at various concns. were investigated in a murine model of respiratory infection (aerosol challenge model). Neonatal mice were more sensitive than young mice to infection by Bordetella **pertussis** after aerosol challenge. In young mice with all vaccines, there were significant differences between immunized mice and control mice. The efficacy of vaccines was increased by the inclusion of addnl. **filamentous hemagglutinin** (**FHA**), **pertussis** toxin (PT), or **pertactin** (PRN) in the basic vaccine (**FHA**:PT:PRN, 7:2:1, wt./wt.). An elevated level of **FHA** strongly increased the efficacy of the vaccine in young mice. It was, however, more difficult to induce protection against B. **pertussis** in neonatal mice than in young mice, irresp. of the levels of the various components in the vaccines. Our data suggest that

**pertussis** vaccines are less effective in neonatal mice than in young mice, as assessed by the aerosol challenge model.

L22 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:121758 HCAPLUS
DOCUMENT NUMBER: 137:61726
TITLE: Characteristics and potency of an acellular **pertussis** vaccine composed of **pertussis** toxin, **filamentous hemagglutinin**, and **pertactin**
AUTHOR(S): Sheu, Gwo-Chang; Wo, Yu-Yuan Peter; Yao, Shu-Man; Chou, Foong-Yuang; Hsu, Tung-Chien; Ju, Chi-Liang; Cheng, Yafen; Chang, Shu-Nien; Lu, Cheng-Hsiung
CORPORATE SOURCE: Center for Disease Control, Department of Health, Vaccine Development Center, Taipei, Taiwan
SOURCE: Journal of Microbiology, Immunology and Infection (2001), 34(4), 243-251
CODEN: JMIIFG
PUBLISHER: Chinese Society of Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In an attempt to develop a safer **pertussis** vaccine, we successfully purified 3 **pertussis** protective antigens-**pertussis** toxin, **filamentous hemagglutinin**, and a 69-kDa outer membrane protein (also named **pertactin**), from Bordetella **pertussis** strain ATCC 9340. The toxicity of **pertussis** toxin could be effectively reduced by the treatment with formaldehyde 0.07% while preserving of a high degree of immunogenicity. By mixing purified **pertussis** antigens with **diphtheria** and **tetanus** toxoids (DT), we have formulated a DT acellular **pertussis** (DTaP) vaccine. Toxicity studies on body-wt. gain in mouse, histamine sensitization, lymphocyte promoting, and Chinese hamster ovary cell clustering tests suggested that this DTaP vaccine is safer than a whole cell vaccine produced in France (DTP[F]). The formulated vaccine elicited high levels of anti-**pertussis** toxin antibodies in both mice and monkeys. In mice, a 2-fold neutralization of anti-**pertussis** toxin antibodies was produced by DTaP compared with DTP(F) vaccine and an acellular vaccine manufd. in Japan (DTaP[J]). More importantly, in intracerebral challenge assay in mouse, this vaccine also provided a better protection than DTaP(J).
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:247205 HCAPLUS
DOCUMENT NUMBER: 134:256900
TITLE: Mucosal DTPa vaccines
INVENTOR(S): Rappuoli, Rino; Pizza, Mariagrazia
PATENT ASSIGNEE(S): Chiron S.p.A., Italy
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001022993 | A2 | 20010405 | WO 2000-IB1440 | 20000928 |
| WO 2001022993 | A3 | 20011025 | | |

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 1223975 A2 20020724 EP 2000-962770 20000928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
JP 2003510292 T2 20030318 JP 2001-526202 20000928
PRIORITY APPLN. INFO.: GB 1999-23060 A 19990929
WO 2000-IB1440 W 20000928

AB Mucosal DTPa vaccines, esp. intranasal vaccines, comprising (a) a **diphtheria** antigen, a **tetanus** antigen and an acellular **pertussis** antigen, and (b) a detoxified mutant of cholera toxin (CT) or E.coli heat labile toxin (LT). Component (b) acts as a mucosal adjuvant. The acellular **pertussis** antigen preferably comprises **pertussis** holotoxin (PT) and **filamentous hemagglutinin** (**FHA**) and, optionally, **pertactin** . The mucosally-delivered combined DTPa formulation is capable of generating a level of protection against B. **pertussis** infection equiv. to that obsd. by alum-adjuvanted parenteral administration. A DTPa vaccine adjuvanted with alum (300 .mu.g/dose, 300 .mu.L vol.) for i.m. administration, for direct comparison with LT-K63-adjuvanted intranasal vaccine(10 .mu.g adjuvant/dose 40 .mu.L vol.). The Pa component of the vaccine included 5 .mu.g rPT, 2.5 .mu.g **FHA**, and 2.5 .mu.g **pertactin**; the T component was 10 .mu.g **tetanus** toxoid; the D component was 10 .mu.g CRM197. The intranasal vaccine enhanced cellular and humoral immune responses to **tetanus** and **diphtheria** as well as **pertussis** antigens. The levels of serum IgG using the intranasal vaccine were equiv. to those obsd. using the i.m. vaccine, but the mucosal immunization advantageously enhance local IgA responses. The protective efficacy of LT-K63-adjuvanted vaccine matched that of the std. alum-adjuvanted vaccine, although clearance kinetics varied slightly.

L22 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:420981 HCAPLUS
DOCUMENT NUMBER: 133:57570
TITLE: Multi-component vaccine comprising at least two antigens from Haemophilus influenzae to protect against disease
INVENTOR(S): Loosmore, Sheena M.; Yang, Yan-ping; Klein, Michel H.
PATENT ASSIGNEE(S): Connaught Laboratories Ltd., Can.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000035477 | A2 | 20000622 | WO 1999-CA1189 | 19991215 |
| WO 2000035477 | A3 | 20001026 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2355466 AA 20000622 CA 1999-2355466 19991215
EP 1140158 A2 20011010 EP 1999-957822 19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002532433 T2 20021002 JP 2000-587796 19991215
PRIORITY APPLN. INFO.: US 1998-210995 A 19981215
WO 1999-CA1189 W 19991215

AB A multi-component immunogenic compn. confers protection on an immunized host against infection caused by Haemophilus influenzae . Such compn. comprises at least two different antigens of Haemophilus influenzae , one of which is an adhesin. High mol. wt. (HMW) proteins of non-typeable Haemophilus influenzae enhance the immune response in a host to a non-proteolytic analog of Hin47 protein in such immunogenic compns. with one component not impairing the immunogenicity of the other. The Haemophilus vaccine may be combined with DTP component vaccines to provide a multi-valent component vaccine without impairment of the immunogenic properties of the other antigens.

IT **7784-30-7, Aluminum phosphate**
**21645-51-2, Aluminum hydroxide**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multi-component vaccine comprising at least two antigens from Haemophilus influenzae to protect against disease)

L22 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:308998 HCAPLUS
DOCUMENT NUMBER: 133:333683
TITLE: A randomized controlled trial with a **diphtheria-tetanus**-acellular **pertussis** (dTpa) vaccine in adults
AUTHOR(S): Van der Wielen, M.; Van Damme, P.; Joossens, E.; Francois, G.; Meurice, F.; Ramalho, A.
CORPORATE SOURCE: Centre for the Evaluation of Vaccination, Epidemiology and Community Medicine, University of Antwerp, Antwerp, Belg.
SOURCE: Vaccine (2000), 18(20), 2075-2082
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this assessor-blinded trial was to compare the immunogenicity and reactogenicity of a candidate **diphtheria**, **tetanus** toxoids and acellular **pertussis** vaccine with reduced antigen content for **diphtheria** and **pertussis** (dTpa) with a licensed reduced adult-type **diphtheria-tetanus** vaccine Td (reduced **diphtheria** content) and with an exptl. candidate monovalent acellular **pertussis** vaccine with reduced antigen content (pa). The dTpa and pa vaccines had identical **pertussis** antigen content. A total of 299 healthy adults (.gtoreq.18 yr, mean age: 30.1 yr .+-. 10.7) were randomized into 3 groups to receive a single dose of one of the study vaccines. In all groups, clin. significant reactions (severe) were infrequent (0-6%) and no serious adverse events were reported during the study. The incidence of local and systemic reactions following the administration of dTpa was comparable to the Td vaccine group. Of the total study group, prior to vaccination 52.3 and 93.2% of the subjects had **antidiphtheria** and anti-**tetanus** antibody levels .gtoreq.0.1 IU/mL, resp.; and 73.1, 98.2 and 74.5% of the subjects were seropos. for **pertussis** toxin (PT), **filamentous hemagglutinin** (**FHA**) and

**pertactin** (PRN) antibodies, resp. One month after vaccination, a similar percentage of subjects in the dTpa and Td groups and anti-**diphtheria** (88.4% vs 90.1%) and anti-**tetanus** (100% vs 98.9%) antibody levels .gtoreq.0.1 IU/mL. Similar anti-**FHA** (100%) and anti-PRN (98.9%) vaccine response rates were seen in the dTpa and pa groups, while the anti-PT vaccine response rates were 96.8 and 100.0%, resp. The dTpa vaccine is as well tolerated and immunogenic as the licensed Td vaccine, and addnl., can also boost antibodies against **pertussis.**

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:792801 HCAPLUS
DOCUMENT NUMBER: 132:333079
TITLE: DTaP vaccines from North American Vaccine (NAVA): composition and critical parameters
AUTHOR(S): Heron, Iver; Chen, F. M.; Fusco, Joan
CORPORATE SOURCE: North American Vaccine Inc., Columbia, MD, USA
SOURCE: Biologicals (1999), 27(2), 91-96
CODEN: BILSEC; ISSN: 1045-1056
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NAVA's acellular **pertussis** vaccine is based on highly purified **pertussis** toxin (PT) inactivated with H2O2. PT was analyzed using advanced biochem. methodol. including mass spectroscopy (LC/MS), yielding mass and peptide mapping information on the subunits. **Pertactin**, adenylate cyclase, and Fim 1, 2 were below detection levels and only trace amts. of **filamentous hemagglutinin** (**FHA**) have been identified as a minor impurity. The vaccine does not induce anti-**FHA** antibodies during the course of a 3-dose primary immunization series in infants. B and T cell epitopes are preserved to a higher extent after H2O2 detoxification when compared with chem. inactivation with formaldehyde, thus providing new information explaining why vaccines employing formaldehyde detoxified PT may need addnl. **pertussis** components added to induce high levels of protection. Anti-PT antibodies generated by NAVA **diphtheria, tetanus**, and acellular **pertussis** vaccine (DTaP) showed a pos. correlation with protection against WHO-defined **pertussis.** The safety profiles for these vaccines showed low reactogenicity with no serious adverse events due to the vaccines. (c) 1999 The International Association of Biological Standardization.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:704686 HCAPLUS
DOCUMENT NUMBER: 130:108839
TITLE: A combined liquid Hib (PRP-OMP), **hepatitis** B, **diphtheria, tetanus** and whole-cell **pertussis** vaccine: uncontrolled preliminary clinical trial of immunogenicity and reactogenicity
AUTHOR(S): Nolan, Terry; Hogg, Geoff; Darcy, Mary-Ann; Skeljo, Maryanne; Carlin, John
CORPORATE SOURCE: Clinical Epidemiology and Biostatistics Unit, Melbourne University Department of Paediatrics, at the Royal Children's Hospital, Melbourne, Australia
SOURCE: Vaccine (1998), 16(20), 2085-2089

CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have conducted a preliminary uncontrolled clin. trial of the immunogenicity and reactogenicity of a new fully liq. pentavalent combination vaccination which incorporates a **diphtheria**, **tetanus** and whole-cell **pertussis** vaccine with Hib (PRP-OMP) and **hepatitis** B vaccines. Forty-five infants received three doses of the pentavalent vaccination at 2, 4, and 6 mo of age, and then a fourth dose at 18 mo of age. Subjects were bled prior to each vaccination, and a month after the third and fourth vaccinations. A 7-day diary card was used to record subject temps. and other systemic and local clin. signs after each vaccination. After the third dose, 98% of subjects had anti-PRP titers above 1 .mu.g mL-1 (95%ci 88%, 100%). Following boosting, the geometric mean titer (GMT) rose a mean 27-fold (95%ci 19-fold, 38-fold) to 33 .mu.g mL-1, and all subjects' titers (lower bound of 95%ci 92%) exceeded 1 .mu.g mL-1. For **hepatitis** B antibody, there was a GMT of 100 mIU mL-1 after the third dose, and 86% of infants (95%ci 73%, 95%) had antibody levels .gtoreq. 10 mIU mL-1. After the fourth dose, there was a mean 77-fold boost (95%ci 48-fold, 130-fold) to a GMT of 860 mIU mL-1 and 95% (95%ci 84%, 99%) of subjects had titers .gtoreq. 10 mIU mL-1. **Diphtheria**, **tetanus**, and **pertussis** antibody levels were all at acceptable levels after the first three doses and again after the fourth vaccination. The pentavalent vaccine was well tolerated at all administration times, and had a minor reactogenicity profile similar to DTPw alone as reported in previous studies. This study has provided preliminary evidence for both the safety and immunogenicity of the pentavalent vaccine given as a course at 2, 4, 6 and 18 mo.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:563409 HCAPLUS
DOCUMENT NUMBER: 129:314703
TITLE: The preterm infant's antibody response to a combined **diphtheria**, **tetanus**, acellular **pertussis** and **hepatitis** B vaccine
AUTHOR(S): Faldella, Giacomo; Alessandroni, Rosina; Magini, Giulia Massinissa; Perrone, Annamaria; Sabatini, Maria Rita; Vancini, Alessandra; Salvioli, Gian Paolo
CORPORATE SOURCE: Preventive Paediatrics and Neonatology, University of Bologna, Bologna, 40138, Italy
SOURCE: Vaccine (1998), 16(17), 1646-1649
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several combined vaccines have recently been developed, in order to improve the implementation of immunization programs and increase the coverage for each vaccine. As the response of preterm infants may vary depending on the vaccination schedule and the vaccine product, it should be evaluated specifically as new vaccines become available. In this study we have examd. the antibody response to a combined **diphtheria**, **tetanus**, acellular **pertussis**, and **hepatitis** B vaccine (DTPa-HBV), given as a primary vaccination course at 3, 5 and 11 mo of postnatal age, in 34 preterm infants (mean gestational age (GA) = 32.0 wk) in comparison with 28 term infants. At the end of the primary course, preterm infants had antibody concns. for **pertussis** 69

kDa antigen and **diphtheria** toxoid that were significantly lower than those of term infants; preterm infants with GA .ltoreq. 31 wk had antibody concns. for **pertussis** 69 kDa **antigen** and **HBsAg** that were significantly lower than those of preterm infants with higher GA; anti-HBs antibody levels correlated with GA. However, the combined DTPa-HBV vaccine elicited seroconversion to all its components in all but two infants, one term and one preterm, after the second dose and a total seroconversion after the third dose. We conclude that preterm infants may be immunized with a combined DTPa-HBV vaccine, starting at the same chronol. age, as term infants.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:563398 HCAPLUS
DOCUMENT NUMBER: 129:314698
TITLE: Antibody and cell-mediated immune responses to booster immunization with a new acellular **pertussis** vaccine in school children
AUTHOR(S): Minh, N. N. Tran; Edelman, K.; He, Q.; Viljanen, M. K.; Arvilommi, H.; Mertsola, J.
CORPORATE SOURCE: Department in Turku, National Public Health Institute, Turku, FIN-20520, Finland
SOURCE: Vaccine (1998), 16(17), 1604-1610
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB School children, 235 healthy 10-12 yr olds, were randomly immunized with either a booster dose of **diphtheria-tetanus**-acellular **pertussis** (dTap) or **diphtheria-tetanus** (dT) vaccine. For this booster immunization designed for school children and adults, the quantities of Bordetella **pertussis** antigens in the dTap vaccine had been reduced to one third of those of the Infanrix vaccine (SmithKline Beecham) commonly used for infants. IgG antibodies and cell-mediated immune (CMI) responses to **pertussis** toxin (PT), **pertactin** (PRN) and **filamentous hemagglutinin** (**FHA**) were assessed by an enzyme immunosorbent assay and in vitro proliferation of peripheral blood mononuclear cells, resp. Before immunization, 55%, 80% and 99% of children had detectable serum IgG antibodies to PT, PRN and **FHA**, whereas CMI response was found in 35%, 27% and 50% of children, resp. After immunization, a 20-30-fold increase in geometric mean level (GML) of antibodies to the **pertussis** antigens occurred and CMI response to PT, PRN and **FHA** was seen in 88%, 94% and 100% of children, resp. Adverse reactions following the immunization were rare. The results show that booster immunization with an acellular **pertussis** vaccine with reduced concns. of antigens induces both antibody and CMI responses and support further studies of this **pertussis** vaccine in school children.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:323156 HCAPLUS
DOCUMENT NUMBER: 129:19687
TITLE: Acellular **pertussis** vaccine with **diphtheria** and **tetanus** toxoids
INVENTOR(S): Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian

PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S. A., Belg.; Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian

SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9819702 | A1 | 19980514 | WO 1997-EP6180 | 19971104 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9853196 | A1 | 19980529 | AU 1998-53196 | 19971104 |
| AU 710475 | B2 | 19990923 | | |
| EP 941117 | A1 | 19990915 | EP 1997-950137 | 19971104 |
| EP 941117 | B1 | 20020828 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI | | | | |
| CN 1236321 | A | 19991124 | CN 1997-199491 | 19971104 |
| BR 9712917 | A | 19991207 | BR 1997-12917 | 19971104 |
| NZ 335384 | A | 20001027 | NZ 1997-335384 | 19971104 |
| JP 2001503422 | T2 | 20010313 | JP 1998-521070 | 19971104 |
| AT 222773 | E | 20020915 | AT 1997-950137 | 19971104 |
| EP 1240905 | A1 | 20020918 | EP 2002-75821 | 19971104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI | | | | |
| ES 2182131 | T3 | 20030301 | ES 1997-950137 | 19971104 |
| ZA 9709984 | A | 19980723 | ZA 1997-9984 | 19971106 |
| TW 471971 | B | 20020111 | TW 1997-86119712 | 19971224 |
| NO 9902156 | A | 19990504 | NO 1999-2156 | 19990504 |
| KR 2000053092 | A | 20000825 | KR 1999-704016 | 19990506 |
| MX 9904278 | A | 20000131 | MX 1999-4278 | 19990507 |
| US 2001014331 | A1 | 20010816 | US 2001-827785 | 20010406 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 1996-23233 | A | 19961107 |
| EP 1997-950137 | A3 | 19971104 |
| WO 1997-EP6180 | W | 19971104 |
| US 1999-284887 | B1 | 19990527 |

AB The invention provides a **diphtheria, tetanus** and **pertussis** vaccine comprising a low dose of each of **diphtheria** toxoid (D), **tetanus** toxoid (T), **pertussis** toxin (PT), **filamentous hemagglutinin** (**FHA**) and **pertactin** (**69K**). The vaccine maintains an ability to prevent **pertussis** while showing exceptionally low reactogenicity. Combination vaccines comprising addnl. antigens are also provided.

IT **7784-30-7, Aluminum phosphate**
**21645-51-2, Aluminum hydroxide**, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(adjuvant; acellular **pertussis** vaccine with

**diphtheria** and **tetanus** toxoids)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:55553 HCAPLUS
DOCUMENT NUMBER: 128:127079
TITLE: Multivalent DTP-polio vaccines
INVENTOR(S): Fahim, Raafat E. F.; Tan, Larry U. L.; Barreto, Luis; Thipphawong, John; Jackson, Gail E. D.
PATENT ASSIGNEE(S): Connaught Laboratories Ltd., Can.; Fahim, Raafat E. F.; Tan, Larry U. L.; Barreto, Luis; Thipphawong, John; Jackson, Gail E. D.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9800167 | A1 | 19980108 | WO 1997-CA472 | 19970702 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2259415 | AA | 19980108 | CA 1997-2259415 | 19970702 |
| AU 9732516 | A1 | 19980121 | AU 1997-32516 | 19970702 |
| AU 714493 | B2 | 20000106 | | |
| EP 914153 | A1 | 19990512 | EP 1997-928089 | 19970702 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| BR 9710460 | A | 19990817 | BR 1997-10460 | 19970702 |
| CN 1228709 | A | 19990915 | CN 1997-197609 | 19970702 |
| JP 2000504032 | T2 | 20000404 | JP 1998-503690 | 19970702 |
| JP 3280675 | B2 | 20020513 | | |
| NZ 333989 | A | 20000623 | NZ 1997-333989 | 19970702 |
| JP 2002069002 | A2 | 20020308 | JP 2001-246781 | 19970702 |
| RU 2194531 | C2 | 20021220 | RU 1999-101850 | 19970702 |

PRIORITY APPLN. INFO.: US 1996-672530 A2 19960702
JP 1998-503690 A3 19970702
WO 1997-CA472 W 19970702

AB A multi-component vaccine compn. is described comprising acellular **pertussis** vaccine components, **diphtheria** toxoid, **tetanus** toxoid, and inactivated poliovirus. The compn. also may contain a conjugate of a capsular polysaccharide of Haemophilus influenzae type b and **tetanus** toxoid or diphteria toxoid, which may be reconstituted from a lyophilized state by the other components of the vaccine. The administration of the multiple component vaccine results in no diminution in the immunogenicity of any component as a result of interference by other components of the vaccine.

IT **7784-30-7, Aluminum phosphate**
**21645-51-2, Aluminum hydroxide**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn., immunogenicity, safety, and clin. effects of multivalent vaccines against **pertussis**, **diphtheria**, **tetanus**, poliomyelitis, and Haemophilus influenzae infection in children in relation to)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:1387 HCAPLUS
DOCUMENT NUMBER: 128:74301
TITLE: Monovalent **pertussis** vaccine and multivalent vaccines against **hepatitis** and Hib using **pertactin**
INVENTOR(S): Slaoui, Moncef Mohamed; Stephenne, Jean
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.; Slaoui, Moncef Mohamed; Stephenne, Jean
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9746255 | A2 | 19971211 | WO 1997-EP2956 | 19970529 |
| WO 9746255 | A3 | 19980108 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9731736 | A1 | 19980105 | AU 1997-31736 | 19970529 |
| EP 928198 | A2 | 19990714 | EP 1997-927150 | 19970529 |
| R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| JP 2000511553 | T2 | 20000905 | JP 1998-500238 | 19970529 |

PRIORITY APPLN. INFO.: GB 1996-11501 A 19960603
WO 1997-EP2956 W 19970529

AB Vaccine compns. comprising the **69K** outer membrane protein of B. **pertussis** (**pertactin**) having 10-100 .mu.g of **69K** per 0.5 mL dose are described for the treatment of whooping cough. Also described are combination vaccines comprising 10-100 .mu.g of **69K** per 0.5 mL, esp. vaccines in which the **69K** component is formulated with **filamentous hemagglutinin** (**FHA**) and **pertussis** toxoid (PT), optionally in combination with one or more other antigens such as **hepatitis** B surface antigen, Haemophilus influenzae b (Hib), injectable polio (IPV) and **hepatitis** A. Methods for prepg. the vaccines are described.

IT **7784-30-7**, **Aluminum phosphate**
**21645-51-2**, **Aluminum hydroxide**, uses
RL: MOA (Modifier or additive use); USES (Uses)
(monovalent **pertussis** vaccine and multivalent vaccines against **hepatitis** and Haemophilus influenza type b using **pertactin**)

L22 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:351280 HCAPLUS
DOCUMENT NUMBER: 127:79909
TITLE: Vaccine- and antigen-dependent type 1 and type 2 cytokine induction after primary vaccination of infants with whole-cell or acellular **pertussis** vaccines
AUTHOR(S): Ausiello, Clara M.; Urbani, Francesca; La Sala, Andrea; Lande, Roberto; Cassone, Antonio
CORPORATE SOURCE: Department Bacteriology Medical Mycology, Istituto Superiore Sanita, Rome, 00161, Italy
SOURCE: Infection and Immunity (1997), 65(6), 2168-2174
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytokine profiles were examd. 1 mo after primary vaccination of infants with a whole-cell **pertussis** vaccine (wP) (Connaught) or either of 2 acellular **pertussis** vaccines, aP-Chiron Biocine (aP-CB) or aP-SmithKline Beecham (aP-SB), each combined with **diphtheria-tetanus** toxoids (DT), in Bordetella **pertussis** antigen-stimulated or unstimulated peripheral blood mononuclear cells (PBMC). **Pertussis** toxin (PT), **filamentous hemagglutinin** (**FHA**), and **pertactin** (PRN) were used as antigens, and the children were defined as responsive when their PBMC proliferated in response to these antigens. The controls were either children who received only DT or children who received **pertussis** vaccine but whose PBMC did not proliferate upon stimulation with B. **pertussis** antigens (unresponsive children). Antigen-stimulated PBMC of responsive wP recipients were characterized by an elevated prodn. of T-helper-cell type 1 cytokines .gamma. interferon (IFN-.gamma.) and interleukin 2 (IL-2), low to minimal prodn. of IL-5, and no prodn. of IL-4. The PBMC of aP vaccine-responsive recipients showed, in addn. to the elevated IFN-.gamma. prodn., a consistent, antigen-dependent prodn. of type 2 cytokines (IL-4 and IL-5), with PRN being the most and PT being the least effective antigen. Type 2 cytokine induction was more pronounced in aP-SB than in aP-CB recipients, as shown by the presence of IL-4 mRNA transcripts and higher IL-5 prodn. in the former (161.6 and 47.9 pg/mL, resp., after PRN stimulation). Appreciable, antigen-unstimulated (constitutive) IFN-.gamma. prodn. was also detected in PBMC cultures of all vaccinees. However, this spontaneous IFN-.gamma. prodn. was, in most vaccines, lower than the antigen-driven cytokine prodn. In contrast, no constitutive type 2 cytokine prodn. was ever obsd. in any vaccine group. PBMC from the 2 control groups (either DT or **pertussis** vaccine recipients) did not show any type 2 cytokine prodn., while IFN-.gamma. prodn. was comparable in both antigen-stimulated and unstimulated conditions. Absence of type 2 cytokines and low levels of constitutive IFN-.gamma. prodn. were also seen in prevaccination children. Thus, **pertussis** vaccines induce in infants a basically type 1 cytokine profile, which is, however, accompanied by some prodn. of type 2 cytokines. The latter are more expressed by aP-SB than by aP-CB recipients, and with PRN than with other antigens, and they are minimally expressed in wP recipients and with PT as antigen. The authors' data also highlight a constitutive IFN-.gamma. prodn. in infancy, which might reflect natural immunization and/or the burden of concomitant vaccinations and which may have an impact on T-helper cell cytokine pattern polarization consequent to **pertussis** vaccination.

L22 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:761878 HCAPLUS

DOCUMENT NUMBER: 126:37038
TITLE: Acellular **pertussis** vaccines and methods of preparation thereof
INVENTOR(S): Vose, John R.; Fahim, Raafat E. F.; Jackson, Gail E. D.; Tan, Larry U. L.; Herbert, Andrew; Boux, Leslie; Barreto, Luis; Thipphawong, John; Klein, Michel H.
PATENT ASSIGNEE(S): Connaught Laboratories Limited, Can.; Vose, John R.; Fahim, Raafat E. F.; Jackson, Gail E. D.; Tan, Larry U. L.; Herbert, Andrew; Boux, Leslie; Barreto, Luis; Thipphawong, John; Klein, Michel H.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9634623 | A1 | 19961107 | WO 1996-CA278 | 19960502 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| US 5877298 | A | 19990302 | US 1995-433646 | 19950504 |
| CA 2220048 | AA | 19961107 | CA 1996-2220048 | 19960502 |
| CA 2220063 | AA | 19961107 | CA 1996-2220063 | 19960502 |
| AU 9654940 | A1 | 19961121 | AU 1996-54940 | 19960502 |
| AU 715417 | B2 | 20000203 | | |
| EP 824358 | A1 | 19980225 | EP 1996-911886 | 19960502 |
| EP 824358 | B1 | 20021204 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| CN 1193324 | A | 19980916 | CN 1996-195229 | 19960502 |
| CN 1198099 | A | 19981104 | CN 1996-195230 | 19960502 |
| JP 11511735 | T2 | 19991012 | JP 1996-532883 | 19960502 |
| EP 1233022 | A1 | 20020821 | EP 2002-77074 | 19960502 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1234579 | A1 | 20020828 | EP 2002-12063 | 19960502 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1234580 | A1 | 20020828 | EP 2002-12064 | 19960502 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| AT 228851 | E | 20021215 | AT 1996-911886 | 19960502 |
| ES 2180758 | T3 | 20030216 | ES 1996-911887 | 19960502 |
| ES 2182971 | T3 | 20030316 | ES 1996-911886 | 19960502 |
| US 2001009666 | A1 | 20010726 | US 1998-945750 | 19980609 |
| US 6399076 | B2 | 20020604 | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 1995-433646 | A | 19950504 |
| US 1995-501743 | A | 19950712 |
| EP 1996-911886 | A3 | 19960502 |
| EP 1996-911887 | A3 | 19960502 |
| WO 1996-CA278 | W | 19960502 |

AB Acellular **pertussis** vaccines comprise purified toxin or toxoid thereof, **filamentous hemagglutinin**, **pertactin** and fimbrial agglutinogens formulated to confer protection to at least 70% of members of an at-risk population. The fimbrial agglutinogens may be prepd. from a Bordetella strain, particularly a B. **pertussis** strain, by a multiple step procedure involving extn. of the fimbrial agglutinogens from cell paste and concg. and purifying the extd. material.

L22 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:71413 HCAPLUS
DOCUMENT NUMBER: 124:115448
TITLE: Genetically-detoxified **pertussis** holotoxin as adjuvants
INVENTOR(S): Gajewczyk, Diane M.; Boux, Heather A.; Novak, Anton; Klein, Michel H.
PATENT ASSIGNEE(S): Connaught Laboratories Ltd., Can.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9534323 | A2 | 19951221 | WO 1995-CA341 | 19950608 |
| WO 9534323 | A3 | 19960118 | | |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2192454 | AA | 19951221 | CA 1995-2192454 | 19950608 |
| AU 9528765 | A1 | 19960105 | AU 1995-28765 | 19950608 |
| EP 764029 | A1 | 19970326 | EP 1995-924122 | 19950608 |
| EP 764029 | B1 | 20020626 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| EP 1149588 | A1 | 20011031 | EP 2001-201598 | 19950608 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1149589 | A1 | 20011031 | EP 2001-201610 | 19950608 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| AT 219686 | E | 20020715 | AT 1995-924122 | 19950608 |
| ES 2179105 | T3 | 20030116 | ES 1995-924122 | 19950608 |

PRIORITY APPLN. INFO.: US 1994-258228 A 19940610
EP 1995-924122 A3 19950608
WO 1995-CA341 W 19950608

AB Compns. contg. genetically-detoxified **pertussis** holotoxin and a non-Bordetella or Bordetella antigen are used as adjuvant for vaccines. The modulated immune response enables immunogenic compns., including multivalent pediatric vaccines such as DTP, to be provided which produce a modulated immune response in the absence of extrinsic adjuvants such as alum. The adjuvanting effect achieved by the genetically-detoxified **pertussis** holotoxin enables at least the same level of adjuvanting effect to be achieved as previously attained by alum, without the undesirable side effects thereof. Also, disclosed are vaccines contg. the adjuvant compn. and other antigen, such as cancer-assocd. antigen and pathogen.

L22 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:80 HCAPLUS
DOCUMENT NUMBER: 120:80
TITLE: **Pertussis** toxin-induced alterations of murine hepatic drug metabolism following administration of **diphtheria** and **tetanus** toxoids and **pertussis**

vaccine adsorbed

AUTHOR(S): Ansher, Sherry; Thompson, Walter; Bridgewater, Jennifer; Snoy, Phil

CORPORATE SOURCE: Div. Bact. Prod., Food Drug Adm., Bethesda, MD, 20892, USA

SOURCE: Infection and Immunity (1993), 61(10), 4240-7
CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Administration of **pertussis** toxin (PT) in combination with **diphtheria** and **tetanus** toxoids adsorbed (DT vaccine) or with acellular **pertussis** vaccine adsorbed and **diphtheria** and **tetanus** toxoids (APDT) elicits dose- and time-dependent alterations in hepatic drug metab. in mice. Cytochrome P 450 (P 450) levels were inhibited more than 50% at 7 days following a single injection of PT mixed with either vaccine. When combined with DT vaccine, 125 ng of PT was required to produce this effect, while as little as 16 ng of PT combined with APDT vaccine inhibited P 450 levels. The inhibition of P 450 levels is similar to that obsd. after a single injection of **diphtheria** and **tetanus** toxoids and **pertussis** vaccine adsorbed (DTP). Alterations of P 450 levels were accompanied by increased activities of quinone reductase but not with changes in plasma interleukin-6 or tumor necrosis factor levels. Other Bordetella **pertussis** virulence factors, such as **filamentous hemagglutinin**, fimbriae and **pertactin**, were also tested but had no significant effect on hepatic drug metab. Endotoxin or prepns. contg. endotoxin caused alternations in hepatic drug metab. within 24 h, concomitant with increased interleukin-6 and tumor necrosis factor levels, but these effects had resolved by 1 wk. DTP vaccine and prepns. contg. PT caused a marked induction of gamma interferon coincident with the maximal inhibition of P 450 levels. This effect was not present with DT or APDT vaccine alone, nor with endotoxin or any combination of factors that did not contain PT. These results demonstrate that PT is a necessary component for the sustained effects of DTP vaccine on hepatic drug metab. and suggest a role for gamma interferon in this process.

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=> d his

     (FILE 'HOME' ENTERED AT 14:36:57 ON 03 SEP 2003)

     FILE 'REGISTRY' ENTERED AT 14:37:04 ON 03 SEP 2003
L1             1 S 287714-41-4/RN

     FILE 'HCAPLUS' ENTERED AT 14:37:28 ON 03 SEP 2003
L2           101 S L1
L3             0 S L2 AND PRD<199902
L4             0 S L2 AND PD<19990201
L5             1 S L2 AND PRD<19990201

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     14:42:37 ON 03 SEP 2003

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     14:42:56 ON 03 SEP 2003
L6            74 S L2

     FILE 'REGISTRY' ENTERED AT 14:44:03 ON 03 SEP 2003
                E FENOFIBRATE/CN
L7             1 S E3

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     14:44:32 ON 03 SEP 2003
L8             2 S L6 AND L7
L9             0 S L6 AND 19990201
L10            1 S L6 AND 1999?
L11            0 S L6 AND 1998?
L12            0 S L6 AND 1997?
L13            3 S L8 OR L10

     FILE 'HCAPLUS' ENTERED AT 15:30:37 ON 03 SEP 2003
                E FLORENT PATRICK/AU
                E STEPHENNE JEAN/AU
                E VANDECASSERIE CHRISTIAN/AU

     FILE 'REGISTRY' ENTERED AT 15:37:40 ON 03 SEP 2003
                E ALUMINUM PHOSPHATE/CN
L14            2 S E3
                E ALUMINUM HYDROXIDE/CN
L15            1 S E3

     FILE 'HCAPLUS' ENTERED AT 15:38:37 ON 03 SEP 2003
L16           18 S ?DIPHTHERIA? AND ?PERTUSSIS? AND ?TETANUS? AND (FHA? OR ?FILA
L17            0 S L16 AND ?HEPATITIS?(W)?SURFACE?(W)?ANTIGEN?
L18            7 S L16 AND ?HEPATITIS?
L19            1 S L16 AND ?ANTIGEN?(3A)HBS?
L20            3 S L16 AND ?IMMUN?(3A)(HIB? OR ?POLIO? OR ?HEPATITIS?(W)A)
L21            4 S L16 AND (L14 OR ?ALUMINUM?(W)?PHOSPHAT? OR L15 OR ?ALUMINUM?(

     FILE 'REGISTRY' ENTERED AT 15:45:34 ON 03 SEP 2003
                E FHA/CN
                E PERTACTIN/CN

     FILE 'HCAPLUS' ENTERED AT 15:46:35 ON 03 SEP 2003
L22           18 S L16 OR L18 OR L19 OR L20 OR L21
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FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT 15:47:06 ON 03 SEP 2003

L23 189 S L22
L24 95 DUP REMOV L23 (94 DUPLICATES REMOVED)
L25 20 S L24 AND (?ADOLESC? OR ?ADULT?)
L26 9 S L24 AND ?BOOSTER?(W)?VACCIN?
L27 28 S L25 OR L26

FILE 'HCAPLUS' ENTERED AT 15:55:57 ON 03 SEP 2003

```
=> d que stat l27
L14           2 SEA FILE=REGISTRY ABB=ON  "ALUMINUM PHOSPHATE"/CN
L15           1 SEA FILE=REGISTRY ABB=ON  "ALUMINUM HYDROXIDE"/CN
L16          18 SEA FILE=HCAPLUS ABB=ON  ?DIPHTHERIA? AND ?PERTUSSIS? AND
                ?TETANUS? AND (FHA? OR ?FILAMENT?(W)?HEMAGGLUT?) AND (?PERTACTI
                N? OR 69K)
L18           7 SEA FILE=HCAPLUS ABB=ON  L16 AND ?HEPATITIS?
L19           1 SEA FILE=HCAPLUS ABB=ON  L16 AND ?ANTIGEN?(3A)HBS?
L20           3 SEA FILE=HCAPLUS ABB=ON  L16 AND ?IMMUN?(3A)(HIB? OR ?POLIO?
                OR ?HEPATITIS?(W)A)
L21           4 SEA FILE=HCAPLUS ABB=ON  L16 AND (L14 OR ?ALUMINUM?(W)?PHOSPHAT
                ? OR L15 OR ?ALUMINUM?(W)?HYDROXID?)
L22          18 SEA FILE=HCAPLUS ABB=ON  L16 OR L18 OR L19 OR L20 OR L21
L23         189 SEA L22
L24          95 DUP REMOV L23 (94 DUPLICATES REMOVED)
L25          20 SEA L24 AND (?ADOLESC? OR ?ADULT?)
L26           9 SEA L24 AND ?BOOSTER?(W) ?VACCIN?
L27          28 SEA L25 OR L26

=> d ibib abs l27 1-28

L27  ANSWER 1 OF 28     MEDLINE on STN
ACCESSION NUMBER:   2003298982     IN-PROCESS
DOCUMENT NUMBER:    22710647   PubMed ID: 12825963
TITLE:              Reduced-antigen combined diphtheria-
                    tetanus-acellular pertussis vaccine
                    (Boostrix).
AUTHOR:             Chapman Therese M; Goa Karen L
CORPORATE SOURCE:   Adis International Limited, Auckland, New Zealand..
                    demail@adis.co.nz
SOURCE:             DRUGS, (2003) 63 (13) 1407-13; discussion: 1415-6.
                    Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY:       New Zealand
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:         Entered STN: 20030627
                    Last Updated on STN: 20030716
AB   The reduced-antigen combined diphtheria-tetanus
     -acellular pertussis vaccine (dTpa) is intended for use as a
     booster dose in individuals aged > or =4 years.  A single dose of dTpa
     elicited generally similar levels of antibodies against pertussis
     antigens (pertussis toxoid [PT], filamentous haemagglutinin [
     FHA] and pertactin [PRN]) as a similar monovalent
     pertussis booster vaccine (ap) in
     adolescents or adults, irrespective of their
     prevaccination serological status or vaccination history.  Levels of
     antibodies directed against diphtheria toxoid were similar in
     recipients of dTpa or a licensed reduced-antigen combined
     diphtheria-tetanus booster vaccine
     (Td).  However, levels of antitetanus antibodies were
     significantly higher in recipients of Td vaccines compared with those
     receiving dTpa.  Similar serological response rates were observed for
     anti-PT, -FHA and -PRN between those receiving dTpa or ap and a
     similar high percentage of recipients of dTpa and the Td vaccines had
     seroprotective levels of antibodies against diphtheria and
     tetanus toxoid.  The most frequently reported local adverse
     reactions following immunisation with dTpa included pain, redness and
     swelling; general symptoms included fatigue, headache and fever.
```

L27 ANSWER 2 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2002394860 MEDLINE
DOCUMENT NUMBER: 22139235 PubMed ID: 12143270
TITLE: [Immunogenicity and reactogenicity of a reduced antigen content **diphtheria, tetanus** and acellular **pertussis** vaccine dTpa) in 10 to 11 years old children and in **adults**]. Inmunogenicidad y reactogenicidad de una vacuna de difteria, tetanos, **pertussis** acelular de contenido antigenico reducido (dTpa) en ninos de 10 a 11 anos de edad y en **adultos**.
AUTHOR: Abarca Katia; Valdivieso Francisca; Potin Marcela; Ibanez Isabel; Vial Pablo
CORPORATE SOURCE: Laboratorio Glaxo SmithKline, Departamento de Pediatria y Centro de Evaluacion de Vacunas, Pontificia Universidad Catolica de Chile.. katia@med.puc.cl
SOURCE: REVISTA MEDICA DE CHILE, (2002 May) 130 (5) 502-10. Journal code: 0404312. ISSN: 0034-9887.
PUB. COUNTRY: Chile
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020730
Last Updated on STN: 20021019
Entered Medline: 20021018

AB BACKGROUND: New vaccination strategies are needed to control the increasing problem of **pertussis** in teenagers and **adults**. AIM: To determine the immunogenicity and reactogenicity of a **diphtheria-tetanus**-acellular **pertussis** (dTpa) vaccine with reduced antigen content. MATERIAL AND METHODS: A single dose of the dTpa vaccine was administered to 60 children 10 to 11 years old and 60 healthy **adults**. At the moment of vaccination and one month later, antibody levels were measured against 3 B **pertussis** antigens: anti-**pertussis** toxin (PT), anti-**pertactin** (PRN) and anti-**filamentous hemagglutinin** (**FHA**), as well as anti-**tetanus** and anti-**diphtheria** antibodies. Local and general symptoms were registered during 14 days following vaccine administration. RESULTS: Antibody response for PT, **FHA** and PRN was 98.3%, 100% and 100% in **adults** and 98.2%, 100% and 98.2% in children. Seropositivity for all **pertussis** antigens was 100% in **adults** and in children one month after vaccination. Geometric mean titers (GMT) significantly increased in **adults** and children. The seroprotection level achieved for **tetanus** and **diphtheria** antibodies one month after vaccination was 96.7% for **adults** and 100% for children, respectively. No serious adverse events were reported during the study. Among local symptoms pain was the most frequent (88-90%), but it was mostly mild or moderate. Solicited general symptoms observed for children and **adults**, respectively, included headache (37% and 53%), fatigue (18% and 35%) gastrointestinal symptoms (18% and 25%) and fever (8% and 3%). Only one vaccinee had fever above 39 degrees C. CONCLUSIONS: The dTpa vaccine showed an adequate safety profile and induced an intense immunological response to all antigens in **adults** and children aged 10-11.

L27 ANSWER 3 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2001641994 MEDLINE
DOCUMENT NUMBER: 21551616 PubMed ID: 11694665

TITLE: Sustained efficacy during the first 6 years of life of 3-component acellular **pertussis** vaccines administered in infancy: the Italian experience.

AUTHOR: Salmaso S; Mastrantonio P; Tozzi A E; Stefanelli P; Anemona A; Ciofi degli Atti M L; Giammanco A

CORPORATE SOURCE: Laboratories of Epidemiology and Biostatistics and Bacteriology and Medical Mycology, Istituto Superiore di Sanita, Rome, Italy. (Stage III Working Group). salmaso@iss.it

CONTRACT NUMBER: N01-AI-25138 (NIAID)

SOURCE: PEDIATRICS, (2001 Nov) 108 (5) E81. Journal code: 0376422. ISSN: 1098-4275.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011107 Last Updated on STN: 20020123 Entered Medline: 20011214

AB BACKGROUND: In 1992-1993, a randomized, double-blind, placebo-controlled clinical trial of two 3-component acellular **pertussis** vaccines was started in 4 of Italy's 20 regions. During the trial, the children had been randomized to receive 3 doses of 1 of 2 acellular **pertussis** vaccines combined with **diphtheria** and **tetanus** toxoids (DT) or of a DT vaccine only, at 2, 4, and 6 months of age. Both **diphtheria-tetanus**-acellular **pertussis** (DTaP) vaccines, 1 manufactured by SmithKline Beecham (DTaP SB; Infanrix) and 1 manufactured by Chiron Biocine (DTaP CB; Triacelluvax), contain **pertussis** toxin (PT), **filamentous hemagglutinin**, and **pertactin**. The results of the first period of follow-up, which ended in 1994 (stage 1), showed that both vaccines had a protective efficacy of 84% in the first 2 years of life; when the trial's follow-up was extended under partial blinding until the participating children had reached 33 months of age (stage 2 of the follow-up), these high levels of efficacy had persisted. Therefore, the objective of this study was to estimate the persistence of protection from 3 to 6 years of age of the 2 3-component DTaP vaccines administered as primary immunization in infancy. METHODS: An unblinded prospective longitudinal study of vaccinated and unvaccinated children in 4 Italian regions, with active surveillance of cough, was conducted by study nurses, and Bordetella **pertussis** infections were confirmed laboratory. The present study (stage 3) included those children who completed stage 2 of the follow-up and were still under active surveillance as of October 1, 1995, accounting for 4217 children who had received DTaP SB (representing 94% of the vaccine's recipients in the initial phase of the trial), 4215 who had received DTaP CB (95% of the original recipients), and 266 who had received DT only (18% of the original recipients). Because the parents of most of the original DT placebo group accepted **pertussis** vaccination during stage 2 in 1995, an additional 856 children were recruited in the DT group at the initiation of stage 3. These additional children were identified from the census list of children born in the same period and living in the same areas as the trial participants but who had been vaccinated in infancy with DT only. Eligible children were included in stage 3 if they had no history of either **pertussis** or **pertussis** vaccination and if a serum sample obtained at the time of enrollment had undetectable immunoglobulin G (IgG) against PT. Parental consent to participate in the study was obtained. Active

surveillance for **pertussis** was conducted in the field by 72 study nurses through monthly contact with each family in the study. A cough episode that lasted >/=7 days was considered to be a laboratory-confirmed infection by Bordetella **pertussis** if at least 1 of the following 5 criteria (listed in hierarchic order) was met: 1) B **pertussis** was obtained from nasopharyngeal culture (culture-confirmed infection); 2) the enzyme-linked immunosorbent assay (ELISA) IgG or IgA titer against PT in the convalescent-phase serum sample increased by at least 100% compared with the acute-phase sample; 3) the PT-neutralizing titers in Chinese hamster ovary assay in the convalescent-phase sample increased by at least 4-fold compared with the acute-phase sample; 4) the ELISA IgG or IgA titer against **filamentous hemagglutinin** in the convalescent-phase sample increased by at least 100% and the culture or the polymerase chain reaction assay on the nasopharyngeal aspirate was negative for B **parapertussis**; and 5) the ELISA IgG PT titer in 1 of the 2 serum samples exceeded the geometric mean titer computed on convalescent sera of the children with a culture-confirmed B **pertussis** infection in each study group. Incidence of laboratory-confirmed B **pertussis** infection, using case definitions that varied in terms of duration and type of cough, was computed and the proportion of cases prevented among DTaP recipients in comparison with DT recipients was calculated. RESULTS: A total of 391 laboratory-confirmed infections were identified in the 3-year follow-up period (138 DTaP SB, 126 DTaP CB, 127 DT recipients, respectively). The mean duration of cough in children with laboratory-confirmed infection was 48, 47, and 70 days for the DTaP SB, DTaP CB, and DT recipients, respectively; the mean duration of spasmodic cough was 15, 13, and 23 days, respectively. When using the primary case definition (ie, laboratory-confirmed B **pertussis** infection and >/=14 days of spasmodic cough or >/=21 days of any cough), the efficacy was 78% for the DTaP SB vaccine (95% confidence interval [CI]: 71%-83%) and 81% for the DTaP CB vaccine (95% CI: 74%-85%). When using the case definition based on a more severe clinical presentation (>/=21 days of spasmodic cough), the vaccine efficacy was 86% (95% CI: 79%-91%) for both vaccines. When using the case definition based on milder clinical presentation (any cough for >/=7 days), the efficacy was 76% (95% CI: 69%-81%) for the DTaP SB vaccine and 78% (95% CI: 72%-83%) for the DTaP CB vaccine. CONCLUSIONS: The persistence of protection through 6 years of age suggests that the fourth DTaP dose could be postponed until preschool age in children who received 3-component acellular **pertussis** vaccines in infancy, provided that immunity to **diphtheria** and **tetanus** is maintained. Additional booster doses could be administered at older ages to reduce reactogenicity induced by multiple administrations and to optimize the control of **pertussis** in **adolescents** and young **adults**.

L27 ANSWER 4 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2001299967 MEDLINE
DOCUMENT NUMBER: 20545884 PubMed ID: 11090714
TITLE: A randomized trial of two acellular **pertussis** vaccines (dTpa and pa) and a licensed **diphtheria-tetanus** vaccine (Td) in **adults**.
AUTHOR: Turnbull F M; Heath T C; Jalaludin B B; Burgess M A; Ramalho A C
CORPORATE SOURCE: Centre for Immunisation Research, The New Children's Hospital, NSW, Westmead, Australia.. fionat@nch.edu.au
SOURCE: VACCINE, (2000 Nov 8) 19 (6) 628-36.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531

AB A single blinded randomized controlled trial to compare the reactogenicity and immunogenicity of **adult** formulated dTpa and monovalent pa vaccines with a licensed Td vaccine. Five hundred and forty-eight healthy **adults** aged 19-70 years received a single injection of dTpa or separate injections of pa or Td (with the alternate vaccine 1 month later). Local and systemic reactions were monitored for 15 days after each vaccination. Serum antibody levels were measured immediately prior to and 1 month after vaccination. Antibody levels were measured 12 months after vaccination in 100 subjects. There was no difference in the total frequency of symptoms and signs between subjects receiving any of the three vaccines. There was a significantly lower incidence of local reactions following pa (60%) than dTpa (80%, P=0.002) or Td (93%, P=0.0008). The incidence of clinically significant (Grade 2 or 3) swelling (> or =20 mm) was higher for Td (20%, P=0.002) than for dTpa (11%) or for pa (2%), however, there were no other significant differences in the incidence of Grade 2 or 3 reactions between the vaccines. A high anti-**pertussis** seroconversion rate (>97%) against all the studied **pertussis** antigens was seen 1 month after vaccination with dTpa and pa. A total of 96 and 99% of subjects receiving dTpa and Td, respectively, had anti-**diphtheria** titres > or =0.01 IU/ml, and all but one subject had anti-**tetanus** titres > or =0.1 IU/ml after 1 month. Twelve months after vaccination the majority (90-100%) of the subjects were still seropositive for each antigen and although GMTs had decreased they were substantially higher than pre-vaccination levels. The dTpa vaccine was well tolerated and capable of eliciting an immune response against all the antigens in a broad spectrum of the **adult** population and could potentially replace Td for routine boosters in **adults**.

L27 ANSWER 5 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000243108 MEDLINE
DOCUMENT NUMBER: 20243108 PubMed ID: 10783014
TITLE: **Adult** formulation of a five component acellular **pertussis** vaccine combined with **diphtheria** and **tetanus** toxoids and inactivated poliovirus vaccine is safe and immunogenic in **adolescents** and **adults**.
AUTHOR: Halperin S A; Smith B; Russell M; Scheifele D; Mills E; Hasselback P; Pim C; Meekison W; Parker R; Lavigne P; Barreto L
CORPORATE SOURCE: Department of Pediatrics, Dalhousie University and the IWK Grace Health Centre, Halifax, Nova Scotia, Canada.. shalperin@iwkgrace.ns.ca
SOURCE: PEDIATRIC INFECTIOUS DISEASE JOURNAL, (2000 Apr) 19 (4) 276-83.
Journal code: 8701858. ISSN: 0891-3668.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20000629
Entered Medline: 20000616

AB BACKGROUND: **Pertussis** is increasingly recognized as an important cause of cough illness in **adolescents** and **adults**. PURPOSE: To evaluate the safety and antibody response to a single dose of an **adult** formulation of a five component (**pertussis** toxoid, **filamentous hemagglutinin, pertactin** , fimbriae 2 and 3) acellular **pertussis** vaccine (aP) combined with **diphtheria** and **tetanus** toxoids (TdaP) and inactivated poliovirus vaccine (TdaP-IPV) in **adolescents** and **adults** and to assess the response to a second dose of the acellular **pertussis** vaccine in a subset of the **adults**. POPULATION AND SETTING: The study addressed 1207 healthy participants (736 **adults** and 466 **adolescents**) recruited in five Canadian communities. STUDY DESIGN: In a randomized, observer-blind, controlled clinical trial, **adult** participants received Td followed at a separate visit by aP, TdaP followed by IPV or TdaP-IPV; **adolescents** received Td-IPV followed at a separate visit by aP or TdaP-IPV. A subgroup of **adults** was given a booster of aP 1 month after TdaP. OUTCOME MEASURES: Antibody titers measured before and 1 month after each immunization; adverse events enumerated at 24 h, 72 h and 8 to 10 days. RESULTS: The aP vaccine given by itself was associated with adverse events less frequently than were Td, Td-IPV, TdaP or TdaP-IPV vaccines, but reaction rates did not differ significantly among the latter products. The antibody response against Bordetella **pertussis** antigens was vigorous in all groups, although **adults** given the TdaP-IPV vaccine had lower antibody titers against **filamentous hemagglutinin, pertactin, diphtheria** and **tetanus** antibodies than those given TdaP vaccine. Similarly **adolescents** given TdaP-IPV had lower antibody titers against **pertussis** toxin, **filamentous hemagglutinin,** fimbriae and agglutinins than those given Td-IPV and aP alone. A second dose of acellular **pertussis** vaccine was not associated with increased adverse events in **adults** but elicited increased antibody titers over that achieved by a single dose only against **pertussis** toxin. CONCLUSIONS: This **adult** formulation five component aP vaccine given as TdaP-IPV is safe and immunogenic in **adolescents** and **adults** and is a candidate vaccine for **adolescent** and **adult** immunization programs.

L27 ANSWER 6 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000182107 MEDLINE
DOCUMENT NUMBER: 20182107 PubMed ID: 10715521
TITLE: A randomised controlled trial with a **diphtheria-tetanus**-acellular **pertussis** (dTpa) vaccine in **adults**.
AUTHOR: Van der Wielen M; Van Damme P; Joossens E; Francois G; Meurice F; Ramalho A
CORPORATE SOURCE: Centre for the Evaluation of Vaccination, Epidemiology and Community Medicine, University of Antwerp, Antwerp, Belgium.
SOURCE: VACCINE, (2000 Apr 14) 18 (20) 2075-82.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20021218
Entered Medline: 20000711

AB The aim of this assessor-blinded trial was to compare the immunogenicity and reactogenicity of a candidate **diphtheria**, **tetanus** toxoids and acellular **pertussis** vaccine with reduced antigen content for **diphtheria** and **pertussis** (dTpa) with a licensed reduced **adult**-type **diphtheria-tetanus** vaccine Td (reduced **diphtheria** content) and with an experimental candidate monovalent acellular **pertussis** vaccine with reduced antigen content (pa). The dTpa and pa vaccines had identical **pertussis** antigen content. A total of 299 healthy **adults** (> or =18 years, mean age: 30.1 years+/-10.7) were randomised into 3 groups to receive a single dose of one of the study vaccines. In all groups, clinically significant reactions (severe) were infrequent (0-6%) and no serious adverse events were reported during the study. The incidence of local and systemic reactions following the administration of dTpa was comparable to the Td vaccine group. Of the total study group, prior to vaccination 52. 3 and 93.2% of the subjects had anti-**diphtheria** and anti-**tetanus** antibody levels > or = 0.1 IU/ml, respectively; and 73.1, 98.2 and 74.5% of the subjects were seropositive for **pertussis** toxin (PT), **filamentous hemagglutinin** (**FHA**) and **pertactin** (PRN) antibodies, respectively. One month after vaccination, a similar percentage of subjects in the dTpa and Td groups had anti-**diphtheria** (88.4% vs 90. 1%) and anti-**tetanus** (100% vs 98.9%) antibody levels > or =0.1 IU/ml. Similar anti-**FHA** (100%) and anti-PRN (98.9%) vaccine response rates were seen in the dTpa and pa groups, while the anti-PT vaccine response rates were 96.8 and 100.0%, respectively. The dTpa vaccine is as well tolerated and immunogenic as the licensed Td vaccine, and additionally, can also boost antibodies against **pertussis**.

L27 ANSWER 7 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000087286 MEDLINE
DOCUMENT NUMBER: 20087286 PubMed ID: 10618527
TITLE: An **adult** formulation of a five-component acellular **pertussis** vaccine combined with **diphtheria** and **tetanus** toxoids is safe and immunogenic in **adolescents** and **adults**
.
AUTHOR: Halperin S A; Smith B; Russell M; Hasselback P; Guasparini R; Skowronski D; Meekison W; Parker R; Lavigne P; Barreto L
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SOURCE: VACCINE, (2000 Jan 31) 18 (14) 1312-9.
Journal code: 8406899. ISSN: 0264-410X.
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ENTRY MONTH: 200003
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AB **Pertussis** is increasingly being recognized as an important cause of cough illness in **adolescents** and **adults**. To evaluate the safety and immunogenicity of an **adult** formulation of a five-component (**pertussis** toxoid, **filamentous hemagglutinin**, **pertactin**, fimbriae 2 and 3) acellular **pertussis** vaccine combined with **diphtheria** and **tetanus** toxoids, we randomly allocated 749 healthy **adolescents** and **adults** from 12-54 years of age recruited from five Canadian communities to receive either **tetanus-diphtheria** vaccine (Td), acellular **pertussis** vaccine (aP) or combined **diphtheria-tetanus**-acellular **pertussis** vaccine (TdaP). Subjects and personnel were unaware of the vaccine allocation. Antibody levels were measured before and one month postimmunization; adverse events were collected at 24 and 72 h and 8 to 10 days. Adverse events were reported in similar frequency amongst the three vaccine groups. Moderate pain at the injection site was reported less frequently in the aP group than the TdaP group (10.7% compared to 19.4%; relative risk 0.6, 95% confidence interval 0.3-0.9). Chills were reported less frequently after Td (5.3%) than after TdaP (12.5%; relative risk 0.4, 95% confidence interval 0.2-0.9). There were no statistically significant differences between recipients of Td and TdaP in **tetanus** and **diphtheria** antitoxin levels achieved. Antibody response against Bordetella **pertussis** antigens was vigorous in all groups although recipients of aP alone had higher levels of antibody levels against **pertussis** toxoid, fimbriae, and agglutinins and lower antibody levels against **pertactin** than did TdaP recipients. We conclude that this **adult** formulation 5-component acellular **pertussis** vaccine is safe and immunogenic in **adolescents** and **adults** and is a candidate vaccine for **adolescent** and **adult** immunization programs.

L27 ANSWER 8 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000085384 MEDLINE
DOCUMENT NUMBER: 20085384 PubMed ID: 10617748
TITLE: Safety and immunogenicity of six acellular **pertussis** vaccines and one whole-cell **pertussis** vaccine given as a fifth dose in four- to six-year-old children.
AUTHOR: Pichichero M E; Edwards K M; Anderson E L; Rennels M B; Englund J A; Yerg D E; Blackwelder W C; Jansen D L; Meade B D
CORPORATE SOURCE: Department of Microbiology, University of Rochester School of Medicine, Rochester, New York, USA..
mepo@uhuratcc.rochester.edu
CONTRACT NUMBER: NO1-AI02645 (NIAID)
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SOURCE: PEDIATRICS, (2000 Jan) 105 (1) e11.
Journal code: 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
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Journal; Article; (JOURNAL ARTICLE)
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LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131

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Entered Medline: 20000114

AB OBJECTIVE: To evaluate the safety and immunogenicity of 6 different acellular **pertussis** vaccines combined with **diphtheria** and **tetanus** toxoids (DTaP) and with 1 licensed whole-cell **pertussis** vaccine (DTwP) as a fifth dose in children who had previously received the same DTaP, a different DTaP, or DTwP as primary and fourth-dose vaccinations. METHODS: Healthy 4- to 6-year-old children were enrolled at 5 National Institute of Allergy and Infectious Diseases Vaccine Treatment and Evaluation Units to receive a fifth dose of a DTaP or DTwP vaccine. All had been randomly assigned to receive 3 primary doses of DTaP or DTwP at 2, 4, and 6 months and a fourth-dose booster at 15 to 20 months of age as part of earlier National Institutes of Health multicenter acellular **pertussis** vaccine trials. Parents recorded the occurrence and magnitude of fever, irritability, and injection site redness, swelling, and pain for 3 days after vaccination. Sera obtained before and 1 month after the **booster vaccination** were analyzed by enzyme-linked immunosorbent assay for antibody to **pertussis** toxin, **filamentous hemagglutinin**, fimbriae, **pertactin**, and **diphtheria** and **tetanus** toxoid. Safety and/or immunogenicity data are reported for 317 children who received DTaP and 10 children who received DTwP. RESULTS: Fever and moderate or severe irritability were uncommon following the fifth dose of DTaP vaccine and were generally less frequent than following the fourth dose. However, for the DTaP vaccine groups, redness, swelling, and pain increased in prevalence compared with the fourth dose. The time course and frequency of reactions following DTaP vaccination were generally similar in children who received the same DTaP, a different DTaP, or DTwP for previous doses in the 5- dose series. No significant differences among the DTaP vaccines were detected in the occurrence of reactions, but the statistical power to detect differences was limited by sample size. Significant increases in antibodies directed against the included antigens were observed for all DTaP vaccines in paired pre- and post-fifth dose sera. Post-fifth dose antibody concentrations differed significantly among the DTaP vaccines. Some children in the study showed an antibody response to an antigen not reported to be in the DTaP vaccine. CONCLUSION: All the studied DTaP vaccines performed similarly with regard to reactions, whether given as a fifth sequential dose of the same vaccine, a mix of different DTaP vaccines in the 5-dose sequence, or after 3 DTwP and 1 DTaP vaccinations. Large injection site reactions occurred more frequently after the fifth dose of DTaP than after the previous 4 doses. A fifth dose of all DTaP vaccines induced an antibody response to those antigens contained in the vaccine. No DTaP was consistently most or least reactogenic or immunogenic.

L27 ANSWER 9 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000070847 MEDLINE
DOCUMENT NUMBER: 20070847 PubMed ID: 10600191
TITLE: DTaP vaccines from north american vaccine (NAVA): composition and critical parameters.
AUTHOR: Heron I; Chen F M; Fusco J
CORPORATE SOURCE: North American Vaccine Inc., Columbia, MD, USA.
SOURCE: BIOLOGICALS, (1999 Jun) 27 (2) 91-6. Ref: 11
Journal code: 9004494. ISSN: 1045-1056.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
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AB NAVA's acellular **pertussis** vaccine is based on highly purified **pertussis** toxin (PT) inactivated with H(2)O(2). PT was analysed using advanced biochemical methodology including mass spectroscopy (LC/MS), yielding mass and peptide mapping information on the subunits. **Pertactin**, adenylate cyclase, and Fim 1, 2 were below detection levels and only trace amounts of filamentous haemagglutinin (**FHA** ) have been identified as a minor impurity. The vaccine does not induce anti-**FHA** antibodies during the course of a 3-dose primary immunization series in infants. B and T cell epitopes are preserved to a higher extent after H(2)O(2)detoxification when compared with chemical inactivation with formaldehyde, thus providing new information explaining why vaccines employing formaldehyde detoxified PT may need additional **pertussis** components added to induce high levels of protection. Anti-PT antibodies generated by NAVA **diphtheria, tetanus** , and acellular **pertussis** vaccine (DTaP) showed a positive correlation with protection against WHO-defined **pertussis**. The safety profiles for these vaccines showed low reactogenicity with no serious adverse events due to the vaccines.


L27 ANSWER 10 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2000054933 MEDLINE
DOCUMENT NUMBER: 20054933 PubMed ID: 10586004
TITLE: Acellular vaccines containing reduced quantities of **pertussis** antigens as a booster in **adolescents**.
AUTHOR: Minh N N; He Q; Ramalho A; Kaufhold A; Viljanen M K; Arvilommi H; Mertsola J
CORPORATE SOURCE: National Public Health Institute, Department in Turku, Finland.. tranminh@utu.fi
SOURCE: PEDIATRICS, (1999 Dec) 104 (6) e70.
Journal code: 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20010521
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AB OBJECTIVE: To evaluate the immunogenicity and reactogenicity of an acellular **pertussis** vaccine (pa) either formulated with **diphtheria** and **tetanus** toxoids (dTpa) or administered consecutively with a licensed **tetanus** and **diphtheria** vaccine (Td) as a 5th dose in **adolescents**. METHODS: A total of 510 healthy children 10 to 13 years of age were assigned randomly, using a single-blind design, to receive either the dTpa vaccine or the Td vaccine with the pa vaccine 1 month later. The quantities of 3 **pertussis** antigens (**pertussis** toxin, **filamentous hemagglutinin**, and **pertactin**) in the dTpa and the pa vaccines were one third of those of the Infanrix vaccine (SmithKline Beecham Biologicals, Rixensart, Beligium) licensed for use in infants. For enzyme-linked immunosorbent assay measurement of serum immunoglobulin

G antibodies and proliferation assay of peripheral blood mononuclear cells, blood samples were obtained before and 1 month after immunization. Local and systemic reactions were recorded on diary cards for 15 days after immunization. RESULTS: After immunization with dTpa or pa, significant and comparable rises in geometric mean values of antibodies (12- to 46-fold) and proliferations (8- to 18-fold) to each of the **pertussis** antigens were noted. After immunization with dTpa or Td, significant rises in geometric mean values of **antidiphtheria** and **antitetanus** antibodies (35- to 76-fold) were noted, and all subjects had values of these antibodies >/=.1 international units/mL. The dTpa and pa vaccines were at least as well tolerated as the licensed Td vaccine. CONCLUSIONS: Booster immunization of **adolescents** with an acellular vaccine containing reduced quantities of **pertussis** antigens in addition to **diphtheria** and **tetanus** toxoids induces good responses in both arms of the immune system without an increase in adverse reactions.

L27 ANSWER 11 OF 28 MEDLINE on STN
ACCESSION NUMBER: 1998379562 MEDLINE
DOCUMENT NUMBER: 98379562 PubMed ID: 9713935
TITLE: Antibody and cell-mediated immune responses to booster immunization with a new acellular **pertussis** vaccine in school children.
AUTHOR: Tran Minh N N; Edelman K; He Q; Viljanen M K; Arvilommi H; Mertsola J
CORPORATE SOURCE: National Public Health Institute, Department in Turku, Finland.. tranminh@utu.fi
SOURCE: VACCINE, (1998 Oct) 16 (17) 1604-10.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
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ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 20000303
Entered Medline: 19981022

AB 235 healthy 10-12 years old school children were randomly immunized with either a booster dose of **diphtheria-tetanus**-acellular **pertussis** (dTap) or **diphtheria-tetanus** (dT) vaccine. For this booster immunization designed for school children and **adults**, the quantities of Bordetella **pertussis** antigens in the dTap vaccine had been reduced to one third of those of the Infanrix vaccine (SmithKline Beecham) commonly used for infants. IgG antibodies and cell-mediated immune (CMI) responses to **pertussis** toxin (PT), **pertactin** (PRN) and **filamentous hemagglutinin** (**FHA**) were assessed by an enzyme immunosorbent assay and in vitro proliferation of peripheral blood mononuclear cells, respectively. Before immunization, 55%, 80% and 99% of children had detectable serum IgG antibodies to PT, PRN and **FHA**, whereas CMI response was found in 35%, 27% and 50% of children, respectively. After immunization, a 20-30-fold increase in geometric mean level (GML) of antibodies to the **pertussis** antigens occurred and CMI response to PT, PRN and **FHA** was seen in 88%, 94% and 100% of children, respectively. Adverse reactions following the immunization were rare. The results show that booster immunization with an acellular **pertussis** vaccine with reduced concentrations of antigens induces both antibody and CMI responses and support further studies of this

**pertussis** vaccine in school children.

L27 ANSWER 12 OF 28 MEDLINE on STN
ACCESSION NUMBER: 1998010670 MEDLINE
DOCUMENT NUMBER: 98010670 PubMed ID: 9346976
TITLE: A safety and immunogenicity comparison of 12 acellular **pertussis** vaccines and one whole-cell **pertussis** vaccine given as a fourth dose in 15- to 20-month-old children.
AUTHOR: Pichichero M E; Deloria M A; Rennels M B; Anderson E L; Edwards K M; Decker M D; Englund J A; Steinhoff M C; Deforest A; Meade B D
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester School of Medicine, Rochester, New York 14642, USA.
CONTRACT NUMBER: NO1-AI05049 (NIAID)
NO1-AI05151 (NIAID)
NO1-AI15096 (NIAID)
+
SOURCE: PEDIATRICS, (1997 Nov) 100 (5) 772-88.
Journal code: 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20010521
Entered Medline: 19971113

AB OBJECTIVE: To compare the safety and immunogenicity of 12 different acellular **pertussis** vaccines combined with **diphtheria** and **tetanus** toxoids (DTaP) with one licensed **diphtheria**, **tetanus**, and whole-cell **pertussis** vaccine (DTwP) as a fourth-dose booster in children who had previously received DTaP or DTwP primary vaccinations. METHODS: Healthy 15- to 20-month-old children were enrolled at six National Institutes of Health Vaccine Treatment and Evaluation Units. All had been randomly assigned to receive three primary doses of DTaP or DTwP at 2, 4, and 6 months of age as part of an earlier National Institutes of Health multicenter trial of DTaP vaccines in the same Vaccine Treatment and Evaluation Units. Parents recorded the occurrence and magnitude of fever; irritability; and injection site redness, swelling, and pain for 3 days after vaccination. Sera obtained before and 1 month after the **booster vaccination** were analyzed for antibody to **pertussis** toxin (PT), **filamentous hemagglutinin** (**FHA**), fimbriae (FIM), and **pertactin** (PRN). **Diphtheria** and **tetanus** toxoid as well as PT neutralizing (Chinese hamster ovary cell) and whole-cell agglutinating antibodies were measured on a subset of sera. RESULTS: A total of 1293 children contributed fourth-dose reaction data. Reactions were less frequent after DTaP than after DTwP. For children vaccinated with a fourth dose of DTaP, which was the same DTaP as received in the primary series, fever and injection site redness, swelling, and pain increased in prevalence compared with the third dose in the primary series. For children receiving DTaP as a fourth dose, injection site redness and swelling occurred more frequently in DTaP-primed than in DTwP-primed children. Variation in the occurrence of reactions among DTaP vaccines was observed. A total of 1160 paired pre-

and postvaccination sera were available for analysis. Serum antibody concentrations before boosting were lower than those obtained 1 month after the primary immunization. After the fourth dose, significant increases in antibodies directed against the included antigens were observed for all vaccines; **postbooster vaccination** antibody titers differed significantly among the DTaP vaccines. For children primed and boosted with the same DTaP, antibody levels were not directly related to the quantity of antigen included for PT, **FHA** , and FIM; for PRN, there was a closer relationship. Some DTaP vaccines given as fourth-dose boosters elicited antibody to PRN or FIM in some vaccinees, although the DTaP vaccines were not reported to contain these antigens; these responses were observed more frequently in DTwP-primed children. Agglutinin antibody rises were observed in all groups immunized with four doses of a DTaP vaccine containing **FHA** or PRN, regardless of whether the vaccine included FIM. **Diphtheria** and **tetanus** antibody levels exceeded the presumed protective concentration (0.1 IU/mL for **diphtheria** and 0.01 IU/mL for **tetanus**) after the fourth dose for all vaccinees. CONCLUSION: Although differences were observed in reaction rates among the DTaP vaccines given as a fourth dose, the DTaP vaccines were, in general, associated with fewer adverse events than a US-licensed DTwP. For DTaP vaccines, fever; irritability; and injection site pain, redness, and swelling occurred more frequently after the fourth dose than after the third dose of the same vaccine in the primary series. No DTaP was consistently most or least reactogenic or immunogenic. Although serologic correlates of **pertussis** immunity are not defined, it is clear that most DTaP vaccines can stimulate comparable or higher serum antibody responses than DTwP for those antigens contained in the vaccine.

L27 ANSWER 13 OF 28 MEDLINE on STN
ACCESSION NUMBER: 97418358 MEDLINE
DOCUMENT NUMBER: 97418358 PubMed ID: 9272363
TITLE: Bordetella **pertussis**-specific Th1/Th2 cells generated following respiratory infection or immunization with an acellular vaccine: comparison of the T cell cytokine profiles in infants and mice.
AUTHOR: Ryan M; Gothefors L; Storsaeter J; Mills K H
CORPORATE SOURCE: Infection and Immunity Laboratory, Maynooth College, Co Kildare, Ireland.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1997) 89 297-305.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971024
Last Updated on STN: 19990129
Entered Medline: 19971015

AB In an investigation of cell-mediated immunity against Bordetella **pertussis**, we found that B. **pertussis** infection in infants and in mice was associated with the induction of antigen-specific T cells that secrete IFN-g and IL-2, but not IL-4 or IL-5. This cytokine profile is characteristic of Th1 cells that mediate cellular immune responses against a range of intracellular pathogens. An examination of cytokine production following immunization with a three-component acellular vaccine, comprising inactive PT, **FHA** and **pertactin** adsorbed to alum, demonstrated that spleen cells from vaccinated mice produced high levels of IL-5, but no detectable IFN-g and

low levels of IL-2. In contrast, peripheral blood mononuclear cells from vaccinated infants produced IL-2, IL-5 and IFN-g. These findings highlight significant differences in the immune responses generated by vaccination and natural infection with B. **pertussis** and demonstrate that the T-cell response induced with an acellular vaccine, although dominated by type 2 cytokines in mice, is more heterogeneous in infants with a Th0 or mixed Th1/Th2 cytokine profile.

L27 ANSWER 14 OF 28 MEDLINE on STN
ACCESSION NUMBER: 97418347 MEDLINE
DOCUMENT NUMBER: 97418347 PubMed ID: 9272352
TITLE: Diagnostic **pertussis** serology in the recent clinical efficacy studies of acellular vaccines.
AUTHOR: Hallander H O
CORPORATE SOURCE: Swedish Institute for Infectious Disease Control, Stockholm, Sweden.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1997) 89 205-12.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971024
Last Updated on STN: 19990129
Entered Medline: 19971015

AB The laboratory routine used and the criteria applied for serological case confirmation in vaccine efficacy trials have a direct influence on the identification of cases, which consequently may also affect the estimation of vaccine efficacy (VE). Some differences in the application of serological confirmation criteria among the recent clinical studies of **pertussis** vaccines include the level of increase in titre and use of single specimen diagnostics. Additionally, the use of pre-exposure serum specimen collections increases the sensitivity of serological confirmation. In the 1992-95 Stockholm trial, a regimen to collect serum samples systematically was introduced; using acute- and convalescent-phase sera from the cough episodes, the proportion of all cases which were serologically confirmed was 25%. When pre-exposure sera were also available, the proportion was 35%; the increased sensitivity was differential by vaccine group and affected the estimated VE to some extent. Therefore, with the different application of serological methods among the various efficacy studies, direct comparisons between studies should be made with great caution.

L27 ANSWER 15 OF 28 MEDLINE on STN
ACCESSION NUMBER: 97262577 MEDLINE
DOCUMENT NUMBER: 97262577 PubMed ID: 9108861
TITLE: Reactogenicity and immunogenicity of a booster dose of a combined **diphtheria**, **tetanus**, and tricomponent acellular **pertussis** vaccine at fourteen to twenty-eight months of age.
AUTHOR: Schmitt H J; Beutel K; Schuind A; Knuf M; Wagner S; Muschenborn S; Bogaerts H; Bock H L; Clemens R
CORPORATE SOURCE: Children's Hospital, University of Mainz, Germany.
SOURCE: JOURNAL OF PEDIATRICS, (1997 Apr) 130 (4) 616-23.
Journal code: 0375410. ISSN: 0022-3476.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 20020125
Entered Medline: 19970508

AB OBJECTIVES: The primary objective was to assess the nature and incidence of adverse events after a fourth dose of a tricomponent acellular **pertussis-diphtheriatetanus** vaccine given in the second year of life after primary vaccination with the same vaccine at 3, 4, and 5 months of age. A secondary objective was to analyze the immunogeniecity of the **booster vaccination**. DESIGN: Of the 5361 children enrolled (aged 14 to 28 months), adverse reactions were specifically solicited from the first 1863 enrollees for the first 4 days after vaccination and then were unsolicited for the remainder of the 4 weeks of follow-up (group 1). In the next 3498 subjects, safety and reactogenicify were entirely unsolicited for this 4-week period (group 2). Immunogenicity was analyzed by means of prebooster and postbooster serum antibody titers for all vaccine components in a random subgroup of 197 children from group 1. RESULTS: Soliciting symptoms elicited reports of at least one symptom in 1314 of 1809 children in group 1 (72.6%), including 993 (54.9%) with local and 885 (48.9%) with general symptoms during the first 4 days after vaccination. When symptoms were gathered in an unsolicited fashion, only 580 of 3498 children in group 2 (16.6%) had a reported symptom during this time, consisting of 344 (9.8%) local and 319 (9.1%) general symptoms, respectively. An unsolicited symptom, areactive edematous swelling of the whole thigh, occurred in 62 children (1.1%), with 45 and 17 reports in groups 1 and 2, respectively. The vast majority of all reported symptoms were mild to moderate, and all children recovered without sequelae. Fourteen serious adverse events were reported, but none was considered to be related to the vaccination. Immunogenicity analysis showed a vaccine response to **pertussis** toxin in 99.5% of subjects, to **filamentous hemagglutinin** in 98.5%, and to **pertactin** (69 kd outer membrane protein) in 99%. All subjects had postvaccination antibody titers of 0.1 IU/ml or greater against **diphtheria** and **tetanus** toxoids.

L27 ANSWER 16 OF 28 MEDLINE on STN
ACCESSION NUMBER: 97051894 MEDLINE
DOCUMENT NUMBER: 97051894 PubMed ID: 8896529
TITLE: Overview of the clinical development of a **diphtheria-tetanus**--acellular **pertussis** vaccine.
AUTHOR: Bogaerts H; Capiau C; Hauser P; Mareschal J C; Melot V; Simons D
CORPORATE SOURCE: SmithKline Beecham Biologicals, Rixensart, Belgium.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1996 Nov) 174 Suppl 3 S276-80.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB A tricomponent acellular **pertussis** vaccine containing **pertussis** toxoid, **filamentous hemagglutinin**, and **pertactin** combined with **diphtheria** and **tetanus** toxoids (DTPa) was developed as a less reactogenic alternative to the traditional whole cell **pertussis** (DTPw) vaccine. In studies of DTPa as a primary vaccination and as a booster dose in DTPa- or DTPw-primed children, the vaccine was safe, well-tolerated, and highly immunogenic; it was less reactogenic than DTPw but at least as immunogenic. A three-dose primary vaccination sequence with DTPa vaccine in the first 6 months of life protects against **pertussis** under conditions of high infectious pressure. These results support the licensing of the vaccine for primary and **booster vaccination** in a growing number of countries. Combined DTPa-based pediatric vaccines are in clinical development.

L27 ANSWER 17 OF 28 MEDLINE on STN
ACCESSION NUMBER: 96384595 MEDLINE
DOCUMENT NUMBER: 96384595 PubMed ID: 8792483
TITLE: Antibody response and reactions to completion of a four-dose series with a two- or three-component acellular **pertussis** vaccine compared to whole cell **pertussis** vaccine.
AUTHOR: Pichichero M E; Green J L; Francis A B; Marsocci S M; Murphy A M; Buscarino C
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Rochester Medical Center, New York 14642, USA.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1996) 28 (2) 159-63.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB We compared the reactions and immunogenicity of DT acellular **pertussis** (DTaP) vaccines containing **pertussis** toxoid (PT) and filamentous haemagglutinin (**FHA**) (2-component DTaP) or PT, **FHA** and **pertactin** (PRN) (3-component DTaP vaccine) with a whole cell (DTwP) vaccine as a fourth-dose booster in 158 children (15-20 months old) who had received 3 primary vaccine doses with the same vaccines at 2, 4 and 6 months of age. Randomization was 3:1 for DTaP:DTwP and all children received concomitant oral polio vaccine (OPV). Fever (> 38 degrees C), irritability, local injection site erythema (> 10 mm), swelling (> 10 mm), and pain (moderate or more) were assessed for 72 h after **booster vaccination**. DTwP vaccinees had a higher incidence of fever (29.4%) and injection-site pain (45.7%) than 3-component DTaP vaccinees (fever, 9.6%, $p < 0.02$; injection-site pain, 3.8%, $p < 0.01$); 2-component DTaP vaccinees had less injection-site pain (8.3%, $p < 0.01$). Pre- and post-vaccination immunoglobulin G (IgG) antibody was measured by enzyme-linked immunosorbent assay (ELISA). Pre- and post anti-PT levels were similar for all 3 vaccine groups. Anti-**FHA** antibody was higher pre- and post-vaccination for both DTaP vaccine groups compared with the DTwP vaccinees ($p < 0.01$ for all comparisons). For 3-component DTaP vaccinees, anti-PRN antibody was higher pre- and post-vaccination compared to DTwP vaccinees ($p < 0.01$ for

both comparisons). **Tetanus** antibody was higher pre- and post-vaccination for DTwP versus both DTaP vaccine groups, and **diphtheria** antibody was similar pre- and post-vaccination for all 3 groups. These 2- and 3-component DTaP vaccines produce less common reactions and comparable or higher antibody to the components they contain (except **tetanus**) than DTwP vaccine when given as a booster to 15- to 20-month-old children previously primed with the same vaccine.

L27 ANSWER 18 OF 28 MEDLINE on STN
ACCESSION NUMBER: 96055299 MEDLINE
DOCUMENT NUMBER: 96055299 PubMed ID: 8522378
TITLE: Serum antibodies to the components of **diphtheria-tetanus-pertussis** vaccine in Polish children related to vaccination status.
AUTHOR: Torbicka E; Lagergard T; Trollfors B
CORPORATE SOURCE: Dept. of Pediatrics, Medical Academy of Warsaw, Poland.
SOURCE: INFECTION, (1995 Jul-Aug) 23 (4) 212-5.
Journal code: 0365307. ISSN: 0300-8126.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960219
Last Updated on STN: 20030222
Entered Medline: 19960125

AB In Poland vaccination against **diphtheria, tetanus** and **pertussis** (DTP) is recommended from 2-3 months of age. Three doses at approximately 6-week intervals are given. A booster dose of DTP is given at 19-24 months and boosters of DT at 6 and 14 years. In this study serum samples were obtained from 166 Polish children aged 2 weeks to 14 years. Vaccination status was verified from the children's Health Books. Antibodies were determined against **pertussis** toxin, **filamentous hemagglutinin** (**FHA**), **pertactin, tetanus** toxoid and **diphtheria** toxin. Antibodies of maternal original against all five antigens were detected in almost all sera from infants not yet vaccinated. Antibody levels increased with the number of vaccinations given. Children who had recently received the fourth vaccination had the highest antibody levels. Antibody levels decreased with time after the fourth vaccination for all antibodies except **FHA**. It was concluded that the Polish whole cell **pertussis** vaccine stimulates antibodies against **pertussis** toxin, **FHA** and **pertactin**, but that antibodies against **FHA** probably also are stimulated by cross-reacting antigens. **Diphtheria** toxin and **tetanus** toxoid antibodies were above protective levels in all vaccinated children, but the long-term decreases justify the booster dose at 14 years. Twenty-five of 166 children (15%) had a vaccination status which deviated from recommendations demonstrating a need to increase the vaccination rate.

L27 ANSWER 19 OF 28 MEDLINE on STN
ACCESSION NUMBER: 93110972 MEDLINE
DOCUMENT NUMBER: 93110972 PubMed ID: 1471424
TITLE: Progress towards the development of new vaccines against whooping cough.
AUTHOR: Rappuoli R; Podda A; Pizza M; Covacci A; Bartoloni A; de Magistris M T; Nencioni L
CORPORATE SOURCE: Immunobiology Research Institute, Siena, Italy.
SOURCE: VACCINE, (1992) 10 (14) 1027-32. Ref: 48

Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930212
Last Updated on STN: 20021218
Entered Medline: 19930128

AB Acellular vaccines against whooping cough are in the final stage of clinical testing and are likely to become available for mass immunization in the near future. Over a dozen vaccines of similar composition have been developed by vaccine companies and research laboratories; all of them contain a detoxified form of **pertussis** toxin (PT) that may be present alone or combined with one or more other non-toxic proteins, such as filamentous haemagglutinin (**FHA**), **pertactin** (69 kDa), and the agglutinogens (AGG). Most of the vaccines contain a PT that has been inactivated by chemical treatment, a process that reduces the immunogenicity of the molecule and may not completely eliminate the risk of reversion to toxicity. To avoid these problems, we have constructed by genetic manipulation a mutant of Bordetella **pertussis** that produces a non-toxic form of PT. This molecule (PT-9K/129G) contains two amino acid substitutions in the S1 subunit (Arg9-->Lys and Glu129-->Gly) which abolish the enzymatic activity of the S1 subunit and all the toxic properties of PT, without changing the immunological properties of the wild-type toxin. Following extensive preclinical studies, which have shown that PT-9K/129G is safe and more antigenic than the toxin treated with chemical agents, this molecule was tested for safety and immunogenicity in **adult** volunteers, 18-month-old children and 2-month-old infants. The molecule has been tested alone, combined with **FHA** and **pertactin** and also combined with **diphtheria** and **tetanus** toxoids.(ABSTRACT TRUNCATED AT 250 WORDS)

L27 ANSWER 20 OF 28 MEDLINE on STN
ACCESSION NUMBER: 93056720 MEDLINE
DOCUMENT NUMBER: 93056720 PubMed ID: 1431261
TITLE: Controlled study of a new five-component acellular **pertussis** vaccine in **adults** and young children.
AUTHOR: Englund J A; Glezen W P; Barreto L
CORPORATE SOURCE: Department of Microbiology and Immunology, Baylor College of Medicine, Houston, TX 77030.
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1992 Dec) 166 (6) 1436-41.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921222

AB A new five-component acellular **pertussis** (AP) vaccine containing 10 micrograms of **pertussis** toxoid, 5 micrograms of

**filamentous hemagglutinin**, 5 micrograms of combined agglutinogens 2 and 3, and 3 micrograms of **pertactin** was evaluated in **adults** and young children. AP vaccine was compared with saline placebo in 31 **adults**, and AP vaccine combined with **diphtheria** and **tetanus** toxoids (ADTP) was compared with whole cell DTP in 41 children, ages 16-20 months, who had received whole cell DTP during infancy. AP was mildly to moderately reactogenic in **adults**, with pain noted within 72 h and 5-8 days after immunization. ADTP was less reactogenic than DTP in children, with significantly decreased pain, redness, irritability, and fever and less use of acetaminophen reported. No late reactions were observed in any child. The multicomponent ADTP was immunogenic, with four-fold or greater antibody rises to at least four **pertussis** antibody assays in all 15 immunized **adults**. **Pertussis**-specific antibody responses in children who received ADTP and DTP were similar. The multicomponent ADTP vaccine is currently being studied in a National Institute of Allergy and Infectious Diseases-sponsored efficacy study in Sweden.

L27 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:226469 BIOSIS
DOCUMENT NUMBER: PREV200300226469
TITLE: DTPa-HBV-IPV/Hib vaccine (Infanrix hexaTM.
AUTHOR(S): Curran, Monique P. (1); Goa, Karen L.
CORPORATE SOURCE: (1) Adis International Limited, 41 Centorian Drive, Mairangi Bay, Private Bag 65901, Auckland, 10, New Zealand: demail@adis.co.nz New Zealand
SOURCE: Drugs, (2003) Vol. 63, No. 7, pp. 673-682. print. ISSN: 0012-6667.
DOCUMENT TYPE: General Review
LANGUAGE: English

L27 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:39680 BIOSIS
DOCUMENT NUMBER: PREV200000039680
TITLE: Local reactions and IgE antibodies to **pertussis** toxin after acellular **diphtheria-tetanus -pertussis** immunization.
AUTHOR(S): Edelman, K. (1); Malmstrom, K.; He, Q.; Savolainen, J.; Terho, E. O.; Mertsola, J.
CORPORATE SOURCE: (1) Department of Paediatrics, Turku University Hospital, FIN-20520, Turku Finland
SOURCE: European Journal of Pediatrics, (Dec., 1999) Vol. 158, No. 12, pp. 989-994. ISSN: 0340-6199.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Local reactions and **pertussis** toxin specific immunoglobulin E antibodies (PT-IgE) were investigated in healthy children following primary and booster immunization with a combined **diphtheria tetanus** acellular **pertussis** vaccine (DTPa) including **pertussis** toxin, filamentous haemagglutinin and **pertactin** . A primary series of DTPa was administered to 150 infants, and 104 of them received a booster dose of DTPa combined with inactivated polio vaccine at 2 years of age. PT-IgE was measured in serum samples from 72 children using a modified nitrocellulose RAST. Primary immunization was associated with low incidence of local reactions (1%-5%). After the booster dose 21% of children had a local reaction gtoreq20 mm. Local reactions after the booster dose tended to be more common in children who

had experienced reaction at primary immunization. PT-IgE was detected in 18% and 86% of children following primary and **booster vaccinations**, respectively. Allergic and non-allergic children did not differ in PT-IgE responses. After primary immunization, elevated PT-IgE levels were found more often in children with a family history of allergy than in those without known allergy in the family. Children with local reactions had significantly higher pre- and post-booster PT-IgE levels and median post-booster **pertactin** IgG and **diphtheria**-IgG levels than children without local reactions. Conclusion: Acellular **pertussis** immunization induces IgE antibodies to **pertussis** toxin, especially after **booster vaccination**. The higher median pre- and post-booster levels of **pertussis** toxin specific immunoglobulin E and post-booster levels of IgG to **pertactin** and **diphtheria** in children with local side-effects reflect a multifactorial immunological mechanism of such reactions.

L27 ANSWER 23 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:394414 BIOSIS
DOCUMENT NUMBER: BA94:66589
TITLE: DEVELOPMENT OF A NEW VACCINE AGAINST WHOOPING COUGH.
AUTHOR(S): NENCIONI L; PIZZA M; BRUGNOLI M; MANETTI R; POPDA A; VANNI R; RAPPUOLI R
CORPORATE SOURCE: R.S. VACCINI, SCALVO, SIENA.
SOURCE: ACTA MED ROM, (1991 (1992)) 29 (1-2), 78-83.
CODEN: AMROBA. ISSN: 0001-6098.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Detoxified **pertussis** toxin (PT) is the main component of all acellular vaccines against whooping cough that have been proposed so far and has been shown to induce protective immunity in children. Most of the vaccines contain a PT that has been inactivated by chemical treatment, a process that reduces the immunogenicity of the molecule and may not completely eliminate the risk of reversion to toxicity. To avoid these problems, we have constructed by genetic manipulation a mutant of Bordetella **pertussis** that produces a non toxic form of PT. This molecule (PT-9K/129G) contains two aminoacid substitutions in the S1 subunit (Arg9 .fwdarw. Lys and Glu 129 .fwdarw. Gly) which abolish the enzymatic activity of the S1 subunit and all the toxic properties of PT, without changing the immunological properties of the wild type toxin. Following extensive preclinical studies which have shown that PT-9K/129G is safe and more antigenic of the toxic treated with chemical agents, this molecule has been tested for safety and immunogenicity in **adult** volunteers. Two studies have been performed, first PT-9K/129G has been tested alone, and then in combination with **FHA** and **69K** , two antigens of Bordertella **pertussis** which are involved in bacterial adhesion. Finally, the same vaccines, either alone or combined with **diphtheria** and **tetanus** toxoide, have been tested in children 12- or 2-4 months old which are the target population for these vaccines. So far, all vaccines tested proved to be safe and very immunogenic both in **adults** and children, indicating that PT-9K/129G is an ideal candidate for a new vaccine against whooping cough.

L27 ANSWER 24 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2003330552 EMBASE
TITLE: Determination of **pertactin** IgG antibodies for the diagnosis of **pertussis**.
AUTHOR: Trollfors B.; Lagergard T.; Gunnarsson E.; Taranger J.
CORPORATE SOURCE: B. Trollfors, Department of Pediatrics, Sahlgrenska University Hospital/East, Goteborg University, S-416 85

Goteborg, Sweden. birger.trollfors@vgregion.se
SOURCE: Clinical Microbiology and Infection, (1 Jul 2003) 9/7 (585-589).
Refs: 16
ISSN: 1198-743X CODEN: CMINFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB .Objective. To compare increases in serum IgG antibody against **pertactin** with increases in IgG against **pertussis** toxin and **filamentous hemagglutinin** (**FHA**) in non-vaccinated children, children vaccinated with **pertussis** toxoid, and **adults**, all with culture-confirmed **pertussis** . Methods. During a double-blind, placebo-controlled, efficacy trial of a monocomponent **pertussis** toxoid vaccine, acute and convalescent sera were obtained from study children and family members with suspected **pertussis**. In the present study, IgG antibodies against **pertactin**, **pertussis** toxin and **FHA** (determined by ELISA) were compared in 207 individuals with culture-verified **pertussis** and paroxysmal cough for .gtoreq.21 days. Results. Significant increases in geometric mean serum IgG against all antigens occurred in non-vaccinated children, but more children responded against **pertussis** toxin and **FHA** than against **pertactin** (96%, 97%, and 62%, respectively). Of the children who had **pertussis** even though they were vaccinated with the **pertussis** toxoid vaccine, 97% responded to **FHA**, while responses to **pertussis** toxin and **pertactin** were less common (68% and 61%, respectively). In the 20 **adults**, the proportions of responders to **FHA**, **pertussis** toxin and **pertactin** were 90%, 80% and 55%, respectively. Conclusion. Determination of IgG against **pertussis** toxin and **FHA** in paired sera in non-vaccinated children with **pertussis** is a more sensitive diagnostic tool than determination of IgG against **pertactin**. **Pertactin** IgG determinations might be of value as a complement to the other antibody assays in vaccinated children and in **adults**.

L27 ANSWER 25 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1999287242 EMBASE
TITLE: **Parapertussis** and **pertussis**: Differences and similarities in incidence, clinical course, and antibody responses.
AUTHOR: Bergfors E.; Trollfors B.; Taranger J.; Lagergard T.; Sundh V.; Zackrisson G.
CORPORATE SOURCE: Dr. E. Bergfors, Goteborg Pertussis Vaccine Trial, St. Paulig 6, S-416 60 Goteborg, Sweden
SOURCE: International Journal of Infectious Diseases, (1999) 3/3 (140-146).
Refs: 25
ISSN: 1201-9712 CODEN: IJIDF3
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology

007 Pediatrics and Pediatric Surgery
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objectives: To compare the incidence, clinical course, and serologic response to Bordetella antigens in patients with **parapertussis** and **pertussis**. Design: Two studies were performed in Sweden during the 1990s, when **pertussis** vaccines were used only in clinical trials. Study I was a retrospective study of patients with positive Bordetella cultures obtained in clinical routine, and study II involved an active search for patients with Bordetella infections during a placebo-controlled trial of a **pertussis** toxoid vaccine. Results: Study I includes 58, and study II 23 patients with **parapertussis** . In study I, the incidence of **parapertussis** was 0.016 cases per 100 person years in children 0 to 6 years old and 0 in older children and **adults**. In study II, the incidence rates of **parapertussis** and **pertussis** were 0.2 and 16.2 per 100 person years, respectively, in children followed from 3 months to 3 years of age. The median number of days with cough was 21 in **parapertussis** and 59 in **pertussis**. The proportions of children with whooping and vomiting were lower in **parapertussis** than in **pertussis** . Geometric mean serum **filamentous hemagglutinin** IgG increased from 6 to 63, and **pertactin** IgG from 4 to 12 units/mL in **parapertussis** patients, which was similar to increases in children with **pertussis**. Conclusions: Disease caused by Bordetella **parapertussis** is diagnosed less commonly and is milder and of shorter duration than disease caused by Bordetella **pertussis**. **Parapertussis** induced serum IgG against **filamentous hemagglutinin** and **pertactin** of similar magnitude as does **pertussis**, and did not induce serum IgG against **pertussis** toxin.

L27 ANSWER 26 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 94330662 EMBASE
DOCUMENT NUMBER: 1994330662
TITLE: [**Pertussis**: New vaccine, new strategy].
LA COQUELUCHE: NOUVEAUX VACCINS, NOUVELLES STRATEGIES.
AUTHOR: Begue P.; Grimprel E.
CORPORATE SOURCE: Hopital Armand Trousseau, Consultation de Pediatrie, Pathologique Infectieuse/Tropicale, 26-28, Av. du Docteur Arnold Netter,75571 Paris Cedex 12, France
SOURCE: Medecine et Hygiene, (1994) 52/2044 (2152-2154).
ISSN: 0025-6749 CODEN: MEHGAB
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: French; English
AB Whooping cough has disappeared in children of those countries that practice mass immunization against **pertussis**. Nevertheless a resurgence was first observed in the United States, and now in France: some **adults** previously immunized are infected again by B. **pertussis** and have contaminated very young susceptible infants. The whole-cell **pertussis** vaccine was poorly tolerated, while the

new cellular vaccines of different composition (P.T. associated to **FHA** and/or **pertactine** and/or agglutinogenes) are immunogenic and have better tolerance. They permit late boosters which are necessary in order to improve immunity in **adults**. If their efficacy is proven by the field trials in progress, the acellular vaccines will replace the whole-cell vaccine for primary immunization in France. Thus, the poorly immunized countries can generalize the **pertussis** vaccine, as did Japan with the acellular vaccine in 80's.

L27 ANSWER 27 OF 28 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-281656 [29] WPIDS
DOC. NO. CPI: C2001-085606
TITLE: Mucosal vaccine to protect against **diphtheria**, **pertussis** and **tetanus**, particularly as booster, contains bacterial antigens and inactivated bacterial toxin adjuvant.
DERWENT CLASS: B04 D16
INVENTOR(S): PIZZA, M; RAPPUOLI, R
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 22
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2001022993 | A2 | 20010405 | (200129)* | EN | 29 |
| RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE | | | | | |
| W: CA JP US | | | | | |
| EP 1223975 | A2 | 20020724 | (200256) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| JP 2003510292 | W | 20030318 | (200321) | | 39 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2001022993 | A2 | WO 2000-IB1440 | 20000928 |
| EP 1223975 | A2 | EP 2000-962770 | 20000928 |
| | | WO 2000-IB1440 | 20000928 |
| JP 2003510292 | W | WO 2000-IB1440 | 20000928 |
| | | JP 2001-526202 | 20000928 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| EP 1223975 | A2 | Based on | WO 2001022993 |
| JP 2003510292 | W | Based on | WO 2001022993 |

PRIORITY APPLN. INFO: GB 1999-23060 19990929
AN 2001-281656 [29] WPIDS
AB WO 200122993 A UPAB: 20010528
NOVELTY - Mucosal DTPa vaccine, comprises (i) **diphtheria** antigen (DAg); (ii) **tetanus** antigen (TAg); (iii) acellular **pertussis** antigen (PAg) and (iv) a detoxified form of either cholera toxin (CT) or Escherichia coli heat-labile toxin (LT).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) Using a detoxified mutant of cholera toxin or Escherichia coli heat labile toxin for use as a vaccine; and
(2) Using a detoxified mutant of cholera toxin or Escherichia coli

heat labile toxin to manufacture an intranasal medicament for **booster vaccination** against whooping cough, **diphtheria** and **tetanus**.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine. Inducing a specific immune response.

USE - The vaccine is used particularly as a booster (following priming by intramuscular immunization) to raise an immune response in a patient, especially a child (claimed), against **pertussis**, **diphtheria** and **tetanus**, but also to treat existing infections. The vaccines can be used to treat the diseases after infection.

ADVANTAGE - The toxin component functions as a mucosal adjuvant, resulting in a vaccine that is as effective as conventional alum-adjuvanted parenteral vaccines. Particularly the new vaccine generates a greater cytokine response to all three antigens, compared with intramuscular injections, with immunoglobulin G responses being essentially the same.

Mice were immunized at 0 and 4 weeks with the triple vaccine, on alum, intramuscularly or (ii) with the triple vaccine containing the K63 LT mutant, intranasally and without alum. Two weeks after the second vaccination, the animals were challenged with an aerosol containing Bordetella **pertussis** W28 (phase I), and the animals examined periodically to determine the number of viable bacteria in the lungs. For both vaccination protocols, the lungs were effectively clear of bacteria 14 days after challenge. An initial intramuscular injection followed by an intranasal booster were equally effective.

Dwg.0/15

L27 ANSWER 28 OF 28 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-286599 [25] WPIDS
DOC. NO. CPI: C1998-088745
TITLE: New vaccine composition - comprises adjuvant and low dose of **diphtheria, tetanus** and acellular **pertussis** antigen(s).
DERWENT CLASS: B04 D16
INVENTOR(S): FLORENT, P; STEPHENNE, J; VANDECASSERIE, C
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
COUNTRY COUNT: 82
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9819702 | A1 | 19980514 | (199825)* | EN | 26 |
| RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW | | | | | |
| W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW | | | | | |
| AU 9853196 | A | 19980529 | (199841) | | |
| ZA 9709984 | A | 19980930 | (199844) | | 26 |
| NO 9902156 | A | 19990504 | (199933) | | |
| EP 941117 | A1 | 19990915 | (199942) | EN | |
| R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI | | | | | |
| CZ 9901640 | A3 | 19991013 | (199949) | | |
| AU 710475 | B | 19990923 | (199951) | | |
| CN 1236321 | A | 19991124 | (200014) | | |
| BR 9712917 | A | 19991207 | (200015) | | |
| HU 9904287 | A2 | 20000428 | (200030) | | |
| NZ 335384 | A | 20001027 | (200062) | | |

MX 9904278 A1 20000101 (200115)
JP 2001503422 W 20010313 (200117) 33
KR 2000053092 A 20000825 (200121)
US 2001014331 A1 20010816 (200149)
EP 941117 B1 20020828 (200264) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
EP 1240905 A1 20020918 (200269) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
DE 69715031 E 20021002 (200273)
TW 471971 A 20020111 (200281)
ES 2182131 T3 20030301 (200322)

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| WO 9819702 | A1 | | WO 1997-EP6180 | 19971104 |
| AU 9853196 | A | | AU 1998-53196 | 19971104 |
| ZA 9709984 | A | | ZA 1997-9984 | 19971106 |
| NO 9902156 | A | | WO 1997-EP6180 | 19971104 |
| | | | NO 1999-2156 | 19990504 |
| EP 941117 | A1 | | EP 1997-950137 | 19971104 |
| | | | WO 1997-EP6180 | 19971104 |
| CZ 9901640 | A3 | | WO 1997-EP6180 | 19971104 |
| | | | CZ 1999-1640 | 19971104 |
| AU 710475 | B | | AU 1998-53196 | 19971104 |
| CN 1236321 | A | | CN 1997-199491 | 19971104 |
| BR 9712917 | A | | BR 1997-12917 | 19971104 |
| | | | WO 1997-EP6180 | 19971104 |
| HU 9904287 | A2 | | WO 1997-EP6180 | 19971104 |
| | | | HU 1999-4287 | 19971104 |
| NZ 335384 | A | | NZ 1997-335384 | 19971104 |
| | | | WO 1997-EP6180 | 19971104 |
| MX 9904278 | A1 | | MX 1999-4278 | 19990507 |
| JP 2001503422 | W | | WO 1997-EP6180 | 19971104 |
| | | | JP 1998-521070 | 19971104 |
| KR 2000053092 | A | | WO 1997-EP6180 | 19971104 |
| | | | KR 1999-704016 | 19990506 |
| US 2001014331 | A1 | Cont of | WO 1997-EP6180 | 19971104 |
| | | Cont of | US 1999-284887 | 19990527 |
| | | | US 2001-827785 | 20010406 |
| EP 941117 | B1 | | EP 1997-950137 | 19971104 |
| | | | WO 1997-EP6180 | 19971104 |
| | | Related to | EP 2002-75821 | 19971104 |
| EP 1240905 | A1 | Div ex | EP 1997-950137 | 19971104 |
| | | | EP 2002-75821 | 19971104 |
| DE 69715031 | E | | DE 1997-615031 | 19971104 |
| | | | EP 1997-950137 | 19971104 |
| | | | WO 1997-EP6180 | 19971104 |
| TW 471971 | A | | TW 1997-119712 | 19971224 |
| ES 2182131 | T3 | | EP 1997-950137 | 19971104 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 9853196 | A | Based on | WO 9819702 |
| EP 941117 | A1 | Based on | WO 9819702 |
| CZ 9901640 | A3 | Based on | WO 9819702 |
| AU 710475 | B | Previous Publ. | AU 9853196 |

| | | | |
|---|---|---|---|
| | | Based on | WO 9819702 |
| BR 9712917 | A | Based on | WO 9819702 |
| HU 9904287 | A2 | Based on | WO 9819702 |
| NZ 335384 | A | Based on | WO 9819702 |
| JP 2001503422 | W | Based on | WO 9819702 |
| KR 2000053092 | A | Based on | WO 9819702 |
| EP 941117 | B1 | Based on | WO 9819702 |
| EP 1240905 | A1 | Div ex | EP 941117 |
| DE 69715031 | E | Based on | EP 941117 |
| | | Based on | WO 9819702 |
| ES 2182131 | T3 | Based on | EP 941117 |

PRIORITY APPLN. INFO: GB 1996-23233 19961107
AN 1998-286599 [25] WPIDS
AB WO 9819702 A UPAB: 19980624
Vaccine composition comprises: (a) **diphtheria** (D), **tetanus**(T) and acellular **pertussis** (Pa) antigens; and (b) an adjuvant. The Pa component comprises **pertussis** toxoid (PT), filamentous haemagglutinin (**FHA**) and **pertactin** ( **69K**). The concentrations of the components per 0.5 ml dose of bulk vaccine are: (i) D ( not more than 5 Lf (not defined)); (ii) T ( not more than 10 Lf); (iii) PT ( not more than 10 mu g); (iv) **FHA** ( not more than 10 mu g), and (v) **69K** ( not more than 4 mu g).

USE - The vaccine may be used against **diphtheria, tetanus** and **pertussis**, and it contains a low dose of each of the components D, T, PT, **FHA** and **69K**. The vaccine may be used for administration to infants, **adolescents** and **adults**.

ADVANTAGE - The vaccine has the ability to prevent **pertussis** while showing exceptionally low reactogenicity.

Dwg.0/14

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=> d his ful

     FILE 'REGISTRY' ENTERED AT 14:37:04 ON 03 SEP 2003
     FILE 'REGISTRY' ENTERED AT 15:37:40 ON 03 SEP 2003
                E ALUMINUM PHOSPHATE/CN
L14             2 SEA ABB=ON  "ALUMINUM PHOSPHATE"/CN
                E ALUMINUM HYDROXIDE/CN
L15             1 SEA ABB=ON  "ALUMINUM HYDROXIDE"/CN

     FILE 'HCAPLUS' ENTERED AT 15:38:37 ON 03 SEP 2003
L16            18 SEA ABB=ON  ?DIPHTHERIA? AND ?PERTUSSIS? AND ?TETANUS? AND
                  (FHA? OR ?FILAMENT?(W)?HEMAGGLUT?) AND (?PERTACTIN? OR 69K)
                  D AU 1-18
L17             0 SEA ABB=ON  L16 AND ?HEPATITIS?(W)?SURFACE?(W)?ANTIGEN?
L18             7 SEA ABB=ON  L16 AND ?HEPATITIS?
L19             1 SEA ABB=ON  L16 AND ?ANTIGEN?(3A)HBS?
L20             3 SEA ABB=ON  L16 AND ?IMMUN?(3A)(HIB? OR ?POLIO? OR ?HEPATITIS?(
                  W)A)
L21             4 SEA ABB=ON  L16 AND (L14 OR ?ALUMINUM?(W)?PHOSPHAT? OR L15 OR
L22            18 SEA ABB=ON  L16 OR L18 OR L19 OR L20 OR L21
     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     15:47:06 ON 03 SEP 2003
L23           189 SEA ABB=ON  L22
L24            95 DUP REMOV L23 (94 DUPLICATES REMOVED)
L25            20 SEA ABB=ON  L24 AND (?ADOLESC? OR ?ADULT?)
L26             9 SEA ABB=ON  L24 AND ?BOOSTER?(W) ?VACCIN?
L27            28 SEA ABB=ON  L25 OR L26
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18 cits from CA Plus — since there were only 18, I provided all of them rather than further limiting as for the other databases

28 cits from "other databases"

I combined L16-L21 with OR so the searched terms would be highlighted.